

Have We Been Here Before?

ON the face of things at least, the expedition to the Moon two weeks ago was a dramatic vindication of those who have managed, in the past eight years, to keep their faith in the Apollo programme. Nobody will grudge the crew of Apollo 15 the congratulations they deserve for their resourcefulness and persistence. Nobody will pretend that the work that they have done is unimportant—the chances are that after a few months of analysis, the samples now returned from the Moon will help to account for many features of the solar system which are at present annoying puzzles. At the same time, however, it is only proper to insist that what appears now to be the crowning achievement of the Apollo programme is neither a justification of the programme of space development on which the National Aeronautics and Space Administration has embarked nor an argument for thinking that still further rockets should be added to the Apollo series. On the contrary, the way in which the programme appears to have reached a plateau of achievement is in many ways an incentive for a closer re-examination of what should happen next. Nobody should be surprised if the problem of how to develop a strategy for NASA, sharpened as it has been by the most recent successful expedition to the Moon, seems an echo of the arguments which marked the early sixties.

So far, the direct outcome of the Apollo programme has been four successful landings on the Moon. In simple money terms, each expedition has cost the best part of \$4,500 million, comparable with the whole expenditure of the National Science Foundation since the Apollo programme was conceived. Even though there is every reason to applaud the recovery of substantial amounts of rock from the surface of the Moon and although it is beyond dispute that the same samples have added in unique ways to the understanding of the astronomy of this part of the Galaxy, much greater benefits have sprung from the less spectacular sponsorship of basic research in the United States which the National Science Foundation, for all its faults, has undertaken. To say this, is not to pretend that the crew of Apollo 15 risked their necks for nothing or even to deny that there are adventitious benefits—spin-offs as the saying goes—from mounting gigantic enterprises like the Apollo programme. The truth is simply that in circumstances in which scientists must share with all other kinds of mortals a sense that few benefits are obtainable without cost, the undoubted benefits of the Apollo programme are not worth what has been spent on them. Moreover, even now that the system is a going concern, the marginal cost of extra expeditions to the Moon is quite substantial. The Apollo programme is reckoned to cost about \$600 million in the financial year that has now begun and will not yield more than two expeditions for such a sum of money. The Glomar Challenger could be operated for the best part of a century on such a budget, and with more valuable results. To acknowledge as much is not in any sense to decry the value of what has been accomplished. It is merely that at a time when all kinds of enterprises for the public good, not simply scientific

enterprises, are starved of funds, there is a case for asking whether extravagance is justifiable.

If, however, there remains a case against the continuation of the Apollo programme after the two landings scheduled for the coming year, there is a very much stronger case against the more ambitious scheme to develop a re-usable shuttle rocket aircraft for carrying people and instruments into orbits about the Earth. In retrospect, it is hard to think that even NASA can be happy with the commitment to this enterprise. The most serious objection to the shuttle project is to know what useful purpose it will accomplish. Two years ago, it is quite clear, the intended function of the shuttle project was to keep NASA's image burning bright. With the impending end of the Apollo programme and with a danger that no amount of success would persuade Congress to continue the exploration of the Moon, NASA considered it would be prudent to have a large and indivisible programme with which to make a claim on public funds. Although there is something in the argument that a single coordinated programme of development is likely to provide a more identifiable focus for the activities of great teams of technical people, the overriding weakness of the concept of the shuttle is that it is almost certain to turn out to be a project which it is more fun to work on than to complete. Briefly, although in theory a re-usable shuttle would be a powerful means of reducing the average cost of a space launching, these benefits are most likely to be apparent for comparatively low orbits about the Earth and are in any case unattainable if there is not a sufficient volume of launching work to do. And even if Congress should allow NASA to go the whole hog and to make a functioning shuttle by the late seventies, it is exceedingly improbable that there will also be money to launch such a large number of orbiting Earth stations that one or two of the shuttle machines could be economically employed on servicing them. Far from being the workhorse of space exploration, the shuttle is well on the way to becoming the white elephant.

Luckily, it now appears that the dogmatic line of the past year is being modified. At the beginning of June, the new administrator of NASA, Dr James C. Fletcher, let it be known that NASA was seriously considering the use of conventional rocket boosters to launch upper stages capable of attaining orbits about the Earth but of returning under their own wings. On this view, it would be possible to keep the cost of the shuttle programme within more modest limits. With luck, the annual cost might be a mere \$1,300 million and not the maximum of somewhere between \$1,600 and \$1,800 million originally expected in 1976–77. This modification, apparently devised by the Grumman Company, is obviously a departure from the simple concept of an entirely re-usable rocket—indeed, not merely would the booster be the lowest stage of a Saturn rocket of the kind used in the Apollo programme but the fuel tanks for the upper stage would also be jettisoned as they were emptied.

By making the shuttle half a shuttle, NASA has also



made it possible for Congress to say that it will pay for one half and not the other. That is what NASA should now admit. And given the possibility that hidden snags may further delay what is, after all, an exceedingly complicated programme, it is entirely possible that the full-blown shuttle, re-usable booster and all, will be a plaything for the eighties, not the seventies. Two years ago, when the project was first launched, such a course was advocated by NASA's critics as the prudent course to take. If events have forced NASA to take this path, so much the better. And it is only fair to say that a comparatively modest approach to the design of the shuttle and in particular the use of the upper stage as a means of testing the recovery of gliding aircraft from a height of 100 miles or so would be technically quite valuable. Whether the same machinery is needed to service the orbiting houses called Skylab is another matter. After all, conventional rockets such as Saturn can do just that. At this point in the development of these advanced programmes, would it not be much more prudent for NASA to aim at a degree of flexibility in its planning? In short, is there not a case for deciding now that the Saturn rocket will remain the workhorse of the large booster programme in the United States, at least until 1975, when prototypes of the shuttle engine will have been flown? That will be soon enough to define the parameters of the next generation of large space rockets. By then, NASA may have a clearer idea of what it wishes to achieve.

What should that be? The first thing to say is that there has never in the past ten years been a scheme for the use of satellites and rockets that compared in attractiveness with the oldest proposal of all for putting satellites to

work—the scheme for communications satellites first suggested by Mr Arthur Clarke immediately after the Second World War. By comparison, even weather satellites are less obvious pieces of machinery, whereas the scheme for using satellites to identify the constituents of the Earth's crust and even to spot corn blight in the Middle West has an air of desperate unreality. The best use so far suggested for Skylab is in X-ray astronomy and, although the scientific community is unlikely to look such a gift horse in the mouth, who would seriously claim that such an expenditure of money will bring a commensurate return? Although in the past two months it must have seemed to NASA that its constituency was being undermined by economic pressures and the scarcity of public money, by technical setbacks (of which there have been precious few) and by the wayward disaffection of American taxpayers, the truth is that its most serious weakness is the lack of an obvious goal at which to aim. In a funny way, NASA is ahead of its time, perhaps even a decade ahead. In the circumstances, it should concentrate on two quite separate objectives. First, there is the development of more sophisticated kinds of rockets for the exploration of the solar system—it is a great misfortune that enterprises such as the Grand Tour of the planets should in present circumstances have to wait until the astrologers say that the planets are properly placed. Second, there is a great deal of useful exploration to be done with existing hardware, near the Earth, on the surface of the Moon and in the directions of the nearer planets. If NASA had the strength to wash its hands of the shuttle except in the most truncated sense, it might yet win back its admired place in the scheme of things.

Throwing in the Sponge

ALL managers of research and development are well aware that the most difficult part of their job is to know when to abandon projects to stop throwing good money after bad. Ever since the managers of research began to acknowledge, in the late fifties and early sixties, that it is possible to set about objectively to understand the process by means of which a bright idea becomes a marketable product, they and those who act as their critics have been on the look-out for ways of codifying the structure of research and development. In the early sixties, the Gibbs-Zuckerman report, originally written as a means of instructing the British Government in the management of its own research facilities, put forward the then fresh discovery that the process of research and development necessarily involves the attrition of bright ideas. A company may set off enthusiastically after a dozen different hares, and may spend quite large sums of money on each of them, but if it is to be reckoned a serious business enterprise, the time will come when it will have to abandon the majority of its research enterprises so as to concentrate on the technical and commercial development of one or two of them. More recently, in the United States, the Charpie report put the same point differently—the successful small companies are those with self-restraint enough to concentrate their energies at the points at which they are likely to be profitable. In Britain, the issue has most recently been taken up by an organization called the Centre for the Study of Industrial Innovation, and in particular Dr W. Duncan Reekie of the University of Edinburgh has set out

to look at a third aspect of the problem—the abandoned projects and the reasons why they were abandoned (Centre for the Study of Industrial Innovation, 162 Regent Street, London W1R 6DD, *On the shelf: a Survey of Industrial R and D Projects Abandoned for Non-Technical Reasons*, £0.50). Unhappily, the report is rich on detail and poor on analysis and generalization, with the result that those who read it will be well supplied with anecdotes that other people have made but perhaps even misled by what the survey has to say about the principles to be adopted in the management of research and development.

The centre was lucky enough to have a good response to a series of enquiries among companies in the United Kingdom—twenty of them were visited and talked to. To read between the lines, the companies concerned seem to have been rather glad of an opportunity of bringing their skeletons out of the cupboard. In a laconic summary of these confessions, the report explains how a company that set out to make an acid-resistant paint found that the research was successful but the price too high, that the successful development of an axial feed pump for feeding water into boilers under pressure had to be abandoned because the only customer changed his mind, a scaled down version of the huge machine that levelled land on highway projects was abandoned because it turned out for one thing to be too expensive for the potential customer and because it was either too heavy or too light for the applications in which its use had been suggested, and a sophisticated system of design for a voltmeter came to

nothing, partly because the sophistication turned out to cost more money than the designers had hoped and partly because the manufacturer, in any case, made quite satisfactory voltmeters in the first place. None of these case studies will surprise those who work in industrial research and development in Britain, the United States or elsewhere. None of them, indeed, will seem anything but a part of the unavoidable ups and downs of commercial life.

In circumstances like these, what morals can be drawn from the abandoned projects described by Dr Reekie? His own conclusions are that the reasons for abandoning a project were usually extrinsic to the company concerned. Sometimes the market would turn out to be too small—and there is some evidence that British companies often find it hard to make a market bigger by promotion. Sometimes companies seem to have embarked on technical developments which were frustrated not merely by changes of mind by monopoly buyers but also without adequate assurance that a potential customer was in a position to buy. Other projects seem to have been abandoned because, when all the figures were available, it turned out that potential competitors were already selling competitively. And then there were problems about uncertainties over the supply of materials or the durability of the product of a successful development campaign. One way and another, Dr Reekie seems to have been given a comprehensive tour of the field in which industrial companies are required by the wish to stay in business to make decisions about the deployment of their resources on research and development.

The flaw in Dr Reekie's paper is its innocence. For decades now, in Britain, it has been customary to wring hands whenever a research project is abandoned, shedding tears not merely for the money that might have been spent elsewhere but for the manpower that has been wasted. In part, the explanation is that technical resources of all kinds were exceedingly scarce in the days immediately after the Second World War, so that there came about a tendency to regard them as a non-renewable resource to be spread as thinly as possible. The result is that even successful research and development projects in Britain are understaffed. Dr Reekie has picked out a few cases on his list where structural weaknesses in the organization of a company account for the failure of a research project, but it is earnestly to be hoped that the appearance of his report will not discourage companies elsewhere from taking the view that abandoned research projects are not merely inescapable, given the uncertainties of commercial life, but that a lack of them probably implies either that too many projects are being carried through to development, with the risk that financial resources will be overstrained, or that nothing worthwhile is happening.

Howzat!

THE grievous condition of cricket, and the agonies of the Marylebone Cricket Club, should not go unremarked simply because British athletes, youths and schoolboys have begun kicking leather balls between upright sticks of wood. In the past year, the pretence has been abandoned that the game of cricket is an open-ended business—teams will open hostilities against each other on a Thursday morning and not be finished until the following

Tuesday. Instead there are now games of cricket in which only a few hours are set aside for play and often all this happens, historians will record with fascination, on Sundays. The whole objective seems to be to make the game more fun to watch without robbing it of that contemplative air which in the past has been calculated to keep the spectators away.

If the managers of the game are serious, they should take more radical steps to keep cricket alive. It is several years now since the Marylebone Cricket Club turned down a proposal for a cricket ball with a moment of inertia much greater than is at present possible, with the result that spin bowlers would be more effective or at least more puzzling to batsmen. There is no reason why it should not in the 1970s experiment with cricket pitches that are shorter, wicket to wicket, than the standard 22 yards (which is, after all, a non-metric measure—who now knows what a chain is?). Presumably batsmen would score less for lack of time to play elegant shots but would on the other hand be able to scamper more quickly between the wickets and be less in danger of being run out. Other innovations that come readily to mind are larger cricket stumps, thinner (or thicker) bats and shorter boundaries. The MCC should give particular attention to the last of these, for it is well known that the spectators are especially delighted whenever a player strikes a cricket ball over the boundary. On the principle of rendering to Caesar what he paid to come to see, is it not time that even bad batsmen were enabled to hit a six?

100 Years Ago



THE GUN-COTTON EXPLOSION AT STOWMARKET

THE disastrous explosion of gun-cotton, which occurred on Friday last on the premises of the Patent Safety Gun-cotton Company, is a calamity of unusual significance. Besides the large number of killed, amounting, we believe, to five-and-twenty persons in all, there were as many as seventy maimed and injured, many of them too, in such a manner as only violent explosions are known to torture and lacerate their victims; and when it is taken into consideration that in all probability a dozen tons of the material actually exploded, the grave nature of the accident is in truth not surprising. The whole group of factory-buildings and out-houses were levelled to the earth at one fell swoop, and for miles away the effect of the catastrophe was acutely felt.

But it is not only from a social point of view that the affair is to be deplored. As a result seriously affecting the science of explosives, the occurrence is peculiarly unfortunate; for the belief in the safety of gun-cotton as an industrial and military agent will now be gravely shaken. It is all very well for scientific men to adduce a plausible reason for the occurrence, and to prove conclusively that with due care and precaution a disaster of this nature could not possibly have happened; but the public unfortunately will not be satisfied with a theoretical assurance of this kind; and indeed measures should certainly be taken, not only to guard against such wholesale death and destruction, but to render the same absolutely impossible.

From Nature, 4, 309, August 17, 1871

OLD WORLD

NUCLEAR WEAPONS

Aldermaston Decision

THE decision that the Atomic Weapons Research Establishment at Aldermaston should be transferred from the Atomic Energy Authority to the Ministry of Defence, anticipated as long ago as April by the Rayner report, was announced on August 5 by Mr John Davies, the Minister for Trade and Industry. This brings to an end a period of great uncertainty at Aldermaston which goes back to the early sixties and the abandonment of the advanced strategic weapons systems then being developed in the United Kingdom—the Blue Streak missile and the warheads that were to have been fitted to the Skybolt air-to-ground missile. For the past few years, it has been increasingly apparent that if Aldermaston has a place anywhere in the British Government's arrangements for research and development, it is with the Ministry of Defence and not the Atomic Energy Authority.

According to the statements last week in the House of Commons and the House of Lords, the government expects that the necessary legislation to transfer the Aldermaston establishment to the Ministry of Defence will have been dealt with in time for the transfer to be complete by the summer of 1972. The government has promised to consult the staff and trade union representatives about how the transfer will affect people's jobs, and Lord Carrington, the Minister of Defence, said that "the general aim will be that the terms and conditions taken as a whole shall be no less favourable than those provided for in existing contracts". At present, something like 19 per cent of the expenditure at Aldermaston concerns projects which are not part of the military programme, and 10 per cent of this work is nuclear in character. The government has been at pains to emphasize that the transfer to the Ministry of Defence will not necessarily reduce the amount of non-military work carried out at Aldermaston, but in future, projects such as those undertaken for the development of the fast reactor programme, will be covered by contracts placed with Aldermaston by the Atomic Energy Authority or one of its dependants.

Mr Anthony Wedgwood Benn, previously responsible as Minister of Technology for the Atomic Energy Authority, complained that it would be dangerous to go against the example shown by most other countries in the West by putting the nuclear weapons research directly under the military, and that the transfer would in any case spoil opportunities for further diversifying the work of the establishment.

So far, there is very little to suggest how the remainder of the Atomic Energy Authority will be affected by the impending reorganization of government research establishments, although a statement last week did say that the government is considering "how best the electricity supply industry and the nuclear industry could be more closely involved in reactor research and development". This formula can, of course, mean anything from the transfer of the reactor development station at Winfrith to the Central Electricity Generating Board, to the amalgamation of the design group of the Atomic Energy Authority with the Central Electricity Generating Board. Now that the fuel manufacturing capacity of the authority has been embodied in British Nuclear Fuels Limited, the way would seem to be open for a daring administrator to bring the Atomic Energy Authority entirely to an end.

SCIENTISTS' PAY

Mighty McCall

MORE than 3,000 disgruntled government scientists gathered in Central Hall, Westminster, last Tuesday in the final meeting organized by the Institution of Professional Civil Servants to protest against the government's pay offer. The purpose of the meeting was to give point to the outrage that scientists in the Civil Service have been expressing about the recent pay award.

Mr William McCall, the general secretary of the IPCS, said that the meeting was the biggest in the history of the IPCS and that there were larger issues behind this dispute. Mr McCall com-

plained that the government was taking advantage of the economic situation and of the extensive unemployment among scientists to depress the pay of scientists. The implications of the government's offer, added Mr McCall, spell disaster for the national economy.

Indirectly, 27,000 scientists are affected by the offer and of these 17,000 are being offered no pay increase (Table 1). Mr McCall claimed that the government's treatment of the pay claim fits into a determined policy to reduce the size of pay increases. The offer of the Civil Service Department, said Mr McCall, was a declaration of war—an attack on the living standards of scientists. No other group in Britain has this year been offered no increase at all, he said; the offer means a cut of 10 per cent in the living standards of scientists. Mr McCall went on to say that as the government employed 27 per cent of all scientists in Britain, its attitude will make the pay of scientists everywhere go down and the ability of the country to make science an attractive profession will be impaired.

Mr McCall also complained that the government has never turned its back so completely on arguments advanced by the IPCS—which does not augur well for the status of the scientist in Britain. The institution's interpretation of the report of the Pay Research Unit differs profoundly from that of the Civil Service Department. Mr McCall pointed out that after investigation by his office it was revealed that the average age of the "equivalent" scientist employed in industry was nine years younger than in the Civil Service. This younger age reflected the better chances of promotion of a man in industry and if nine incre-

Table 1 The IPCS Claim and the Government's Offer

Numbers involved	Present scale	IPCS claim	Government offer
Principal Scientific Officer 1,700	3,902 max 2,820 min	4,208 (7.8%) 3,174 (12.6%)	nil
Senior Scientific Officer 1,200	2,703 2,193	3,398 (25.6%) 2,483 (13.2%)	nil
Scientific Officer 600	1,982 1,162	2,077 (4.8%) 1,486 (27.9%)	2.2% 9.7%
Chief Experimental Officer 300	3,873 3,258	4,208 (8.6%) 3,714 (14.0%)	nil
Senior Experimental Officer 2,100	3,099 2,529	3,396 (9.6%) 2,849 (12.7%)	nil
Experimental Officer 3,900	2,177 1,725	2,583 (18.6%) 1,973 (14.4%)	nil
Assistant Experimental Officer 1,500	1,578 741	2,077 (31.6%) 1,196 (26.4%)	nil 9.9%
Senior Scientific Assistant 1,200	1,777 1,367	2,077 (16.9%) 1,579 (15.5%)	nil 2.4%
Scientific Assistant 4,500	1,253 490	1,450 (15.7%) 550 (12.2%)	5.7% 7.1%

ments were added to the salary of the government scientist it would then be a fair comparison.

One of the implications of this offer that worries the IPCS is that it will not be practical to implement the Fulton report on the restructuring of the Civil Service if the scientists' salaries fall much below those of the equivalent grades in the administration and engineering classes. If the Principal Scientific Officer gets no increased offer then his salary will be £500 less than the other grades within the service and an amalgamation of the grades will thus prove impossible.

Mr McCall was given a tumultuous acclamation by the scientists that packed the hall. The meeting, however, could only be regarded as a show of strength as no better offer was received by the IPCS before the official tribunal sat yesterday, August 12, to arbitrate the dispute. Mr M. J. Mustill, QC, the chairman, is expected to announce the tribunal's decision early next week and Mr William McCall will certainly be a very disappointed man if no better offer than that already made by the government is recommended.

ENZYME RESEARCH

More Chemists Needed

THE Science Research Council has come out with a declaration that more should be done to interest undergraduates in enzyme chemistry and technology and that practising chemists should be encouraged to devote their special skills to the subject. These points emerge from a review carried out by the Enzyme Chemistry and Technology Committee of the Science Research Council (*Support of Enzyme Chemistry and Technology 1969-71*, Science Research Council, 1971). The committee, under the chairmanship of Professor Sir Ewart Jones, was set up in 1969 following recommendations of a specialist panel of the Science Board.

The continuing importance which the SRC attaches to interdisciplinary research is indicated by the extension of the original two year life of the committee to four years. Since the beginning, the committee has recommended the award of forty-four research grants, of which the largest was £371,000 for the establishment of the Enzyme Group at Oxford. The committee makes no apology for its decision to award five of the grants over periods as long as five years, because it considers that long term funding in suitable circumstances increases the possibility of recruiting really competent staff and encourages the full and unhindered development of new ideas. But several applications have been turned down be-

cause they did not involve sufficiently close collaboration between disciplines.

Although fourteen research studentships a year have been made available to the committee for distribution to its grantees, the review makes it clear that the chance of obtaining more training grants specifically for enzyme chemistry and technology is slim. But as industry begins to play a useful role (and the interest of Whatman Biochemicals in enzyme purification is a case in point) it should be possible to make more use of the SRC's Cooperative Awards in Pure Science. And workers in enzyme chemistry can still apply for the research studentships meted out by the Chemistry, Chemical Technology and Biology Committees of the SRC. Not surprisingly the committee is trying to encourage the teaching of enzyme mechanisms in university courses and it suggests that enzyme isolation, purification and reactions should form part of some undergraduate practical courses.

On research grants, the committee says that many aspects of the subject are still failing to attract sufficient grant applications. Enzyme isolation and the production of pure enzymes and cell abstracts are two examples. The SRC is already partially supporting the extension of facilities at the Microbiological Research Establishment, Porton, so that the availability of partially purified enzymes can be increased, but the committee is particularly keen to encourage more proposals for work on enzyme separation procedures, especially those involving chromatographic methods.

The structural study of enzymes was singled out in the original SRC panel report as an important feature of the continued development of enzyme chemistry and there seems to be no lack of suitable applications. Funds have been provided for a high field NMR spectrometer for the Oxford group and some instrument time will eventually be made available to others working on biological problems. The committee has also been consistently of the opinion that studies of peptide synthesis are essential to the understanding of enzyme mechanisms and the review calls for more fundamental work to be done; it cites the problems of the unambiguous formation of disulphide cross-linkages, the protection of histidine and the incorporation of tryptophan as worthy of further investigation.

The application of enzymes in industrial processes is still apparently a completely open field and it is impossible to say in what ways the unique reaction-mediating properties of enzymes will be used. The SRC has awarded grants to three groups working on the attachment of enzymes to solid supports (for example, a chromatographic column or

a glass tube) and this kind of research could lead to the production of viable systems which use enzymes to catalyse chemical processes that are difficult to perform by conventional means.

METRICATION

Waiting for a Policy

THE announcement (see page 439) that the United States Department of Commerce is recommending metrication to Congress may make some reluctant British companies finally decide to change to the metric system. Several companies which have been exporting their goods to the United States have so far resisted the British Metrication Board's entreaties to go metric, and this has been a major stumbling block to the process that was started in 1965. Very few countries have not so far either changed to the metric system or made a firm commitment to do so. The United States is, of course, the largest country that has not yet decided to change, and it keeps company with such bastions of the imperial system of measurement as Barbados, Burma, Gambia, Liberia, Muscat and Oman, Nauru, Sierra Leone, Southern Yemen, Tonga and Trinidad.

What progress has been achieved in Britain during the past six years? The aim was to convert British industry to the metric system by the end of 1975. The British Standards Institution, taking the construction industry as an example, reports that nearly all the companies involved with public contracts have already changed and that two thirds of the others have either changed or are scheduled to change. Elsewhere, most larger companies have made the change and the smaller and middle sized companies are thinking of following suit.

In Britain, there is as yet no legislation to compel change by 1975 or any other date. Moreover, the Metrication Board is required to work chiefly by exhortation. The original aim, decided by the British Standards Institution in collaboration with industry, was that 75 per cent of all companies in Britain should convert by 1975, and the institution reports that this will be achieved at the present rate; it even hopes that the final figure will be more like 85 per cent.

The advantages of metrication to industries involved in overseas trade are self-apparent, but what are not very clear are the advantages to industries that do not export. The British Standards Institution is finding that companies that have converted have saved a great deal of money in the metric rationalization process. The philosophy that the costs of metrication

"lie where they fall" has not encouraged such companies to go metric, but the many examples of cost saving that are now becoming obvious, together with the realization that in the near future components made to imperial standards will cost more, are making many companies rethink their policy.

If the industrial sector is well on the way to its original aim, there is a serious delay in the public and educational sectors. The present government has not been over-enthusiastic about metrication but has not, on the other hand, made any decisions to alter course. A White Paper on metrication that will spell out the government's policy has been expected for some time, but it will not appear at least until Parliament returns after the summer recess. The original intention was to introduce metric road signs in 1973, but Mr John Peyton, Minister for Transport, announced in late 1970 that this will not now be the case and that the government has no alternative date in mind.

There is no doubt that a definite statement of government policy is needed to reassure educationists who are already heavily committed to metrication. After 1972, all school examinations will be set in metric units and the SI system of units will be universally accepted. Text-books have also been rewritten to conform with these standards. If a change of government policy towards metrication in education is expressed in the White Paper it will, as a spokesman of the National Union of Teachers said this week, cause consternation.

BUILDING RESEARCH

Constructive Policies

THE Building Research Station, now under entirely new management—at least in name—looks likely to spend almost £2½ million in the financial year 1970–71, according to the annual report (*Building Research Station 1970*, HMSO, 85p). The station, which is at Garston, Hertfordshire, and its Scottish Laboratory, now fully established in new quarters at East Kilbride, is the construction research arm of what used to be the Ministry of Public Building and Works. In the reorganization of central government last autumn, however, the BRS, in company with the Road Research Laboratory, came under the wing of the new Department of the Environment.

The BRS is chiefly concerned with research into environmental design—for example, sound insulation techniques, the design of safe buildings and ways of mechanizing their construction and the performance and improvement of building materials. All of these interests are well illustrated by the Finchampstead project where the con-

struction of 172 houses was planned and analysed along BRS lines. One measure of the success of this project is the estimated 900 man-hours required for each dwelling. A recent survey has shown that 1,200 man-hours per house is a more usual figure. The BRS provides an advisory unit, established in May 1970, and of course the station is the technical agent for the Agrément Board which takes responsibility for the testing and approval of new building materials.

On the international front, the station has recently played an important part in the sale of a 5,000-tonne hydraulic press to the Yugoslavian Government. The press, worth about half a million pounds, was designed and built at Garston by a consortium of interests including the BRS called Go-Con Concrete Ltd and is used for the rapid production of large concrete panels. Finance for the construction of the press was arranged with the help of the National Research and Development Corporation.

ELECTRICITY SUPPLY

Computing the Future

PLANNING the development of an electricity supply system so that costs are kept to a minimum can no longer be carried on without a computer. Both the Central Electricity Generating Board in Britain and the Commission of the European Communities now make extensive use of computing methods to decide the optimum mix of the types of power plant at present available or expected to prove themselves before the end of the century.

When only coal-fired plant was available, planning entailed the solution of a classic problem in operational research—how to place a number of coal-users in such a way that the cost of transporting coal from the coalfield was minimized. But the evolution of oil-fired and nuclear plant and the increasing use of gas turbines for meeting peak demand have considerably complicated the problem. Planning now involves not only the estimation of the distribution of demand throughout the year but also the relative capital and running costs of different types of plant and some prediction of the way in which nuclear technology is likely to develop.

The approaches to the problem which have been adopted by the CEGB and the research group at the Joint Research Centre at Ispra (where the European research is being carried out) are somewhat different. Both aim to evolve a plan for the next thirty years or so which can be continually updated, but the work at Ispra takes more detailed account of the possible development of nuclear technology.

The whole problem is a system analyst's 'dream. The CEGB programme, for example, has been evolved over a period of about ten years and contains an expression for the total cost of electricity during a given year. The objective is to minimize this expression under the applied constraints such as government regulations about the use of capital and the cost and availability of fossil fuels.

Several factors have to be taken into account in setting up the expression for the cost. The total amount of generating capacity which must be available is, of course, determined by the peak demand even though this may last for only a few days and at first sight there is an obvious merit order for power plants which is bound to affect the distribution between the different types. Nuclear plants are the cheapest to run, followed by oil, coal and gas turbine. On the other hand, the order of capital costs is reversed; gas turbine plants are the cheapest and the capital cost of a nuclear station can be about fifty per cent higher than that of an oil-fired station of comparable capacity. The philosophy behind the programme is that the type of generator with the cheapest running cost should supply electricity for as much of the year as possible and that the more expensive forms of power generation should only be used to meet the higher power demands that occur for short periods of the year. As more and more of the plant with the cheaper running costs is introduced into the system, the more expensive and older plant can be run for shorter periods and eventually phased out. The CEGB programme has predicted the future power plant mix shown in the Table.

Generator Plant Mix predicted by the CEGB Programme

Year	Nuclear	Conventional
1975	13%	87%
1980	>20%	<80%
2000	60%	40%

Although the computer work at Ispra is along similar lines, it is in many ways more detailed. Among its predictions for the European electricity supply industry are that the amount of electricity generated by non-nuclear means will level off in 1985 but will increase again in 1995 when more capacity will be required to supply electricity in the peak periods. The use of fast reactors will increase at the maximum rate soon after their introduction (estimated to be in 1985) but after a further fifteen years or so, the growth rate will be determined chiefly by the rate of increase of the power demand. The progress made by the high temperature re-

SRC Members

THE Science Research Council has announced the appointment of six new members to its research boards so as to make up for the regular retirement of previous members. On the **Astronomy Space and Radio Board**, Professor J. Ring (Imperial College, London) and Mr M. O. Robins (Ministry of Aviation Supply) replace Mr R. Lees (Ministry of Aviation Supply) and Professor P. A. Sheppard (Imperial College, London). On the **Engineering Board**, Professor G. D. S. MacLellan (University of Leicester), Professor R. J. A. Paul (University College of North Wales) and Professor R. W. H. Sargent (Imperial College, London) replace Professor J. G. Ball (Imperial College, London), Mr H. R. Galleymore (Procter & Gamble Limited) and Dr M. R. Gavin (Chelsea College of Science and Technology). On the **Nuclear Physics Board**, Professor R. G. Chambers (University of Bristol), Professor L. L. Green (University of Liverpool) and Dr K. F. Riley (University of Cambridge) replace Professor W. E. Burcham (University of Birmingham), Sir Derman Christopherson (University of Durham) and Dr K. Mather (University of Southampton). Dr T. Emmerson (Guest, Keen and Nettlefolds Limited) and Professor Sir Ronald Nyholm (University College, London) have retired from the **Science Board** but no new appointments have been made.

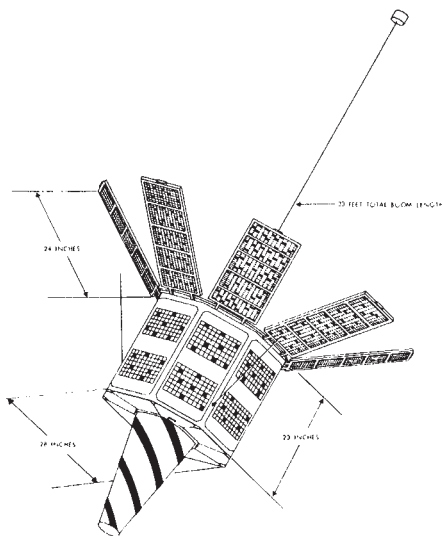
actors is expected to be determined almost entirely by comparisons with the fast breeder reactor during development and the installed capacity will not increase at all once the fast breeder reactor becomes established.

METEOROLOGY

Come in Please, No. 24

A WEATHER satellite that obtains its data not from cameras but by the interrogation of automatic sensors carried into the atmosphere by balloons is to be launched next week. The balloons will take the sensors into a region which, because of its remoteness, is *terra incognita* on weather maps—the oceans of the southern hemisphere.

Although the satellite is experimental in the sense that the electronic system to be used for collecting data has not been applied before, the experiment is on a sufficiently large scale to make a significant contribution to the World Weather Programme. Five hundred



The French Eole weather satellite. The long boom is the gravity gradient stabilization system, so that the conical spiral antenna for balloon interrogation and data collection points towards the Earth.

sensors and balloons are available for launch from three locations in Argentina at latitudes of 33°, 39°, and 55° S by the French Centre Nationale d'Etudes Spatiales, which also developed the satellite to be launched on or after August 16 by NASA.

In previous trials, balloons launched from southern hemisphere stations have lasted for several months, circumnavigating the Earth several times until lost because of icing. The French satellite carries a 4 Watt, 464 MHz transmitter for the interrogation of the balloon-borne sensors, a receiver for collecting the data transmitted by the sensors, and a 136 MHz transmitter for relaying the data to ground stations.

The philosophy of the experiment seems to be the recognition that in spite of the impact that pictures of cloud cover from conventional weather satellites have had on weather analysis and forecasting, there is still an urgent need for more measurements of temperature, pressure and wind speed which ground stations provide. In the absence of a technique that allows pressures and wind speeds in the lower atmosphere to be measured directly from sensors on satellites, the approach being tried by CNES and NASA is the most promising way of obtaining data from remote areas that are of meteorological interest.

Although the techniques of communications satellites have been used before for the collection of data from automatic sensors, the French system is an important advance on earlier American experiments because of its large capacity, allowing the tracking of as many as 500 balloons. It will be possible to determine the horizontal location of the balloons to the nearest 3 km (their vertical position will be

governed by their inflation pressure so that they float at 11.85 km), a considerable improvement on a similar data collection system that has been tested on the Nimbus satellites and better by far than tracking from the ground.

EASTERN SCIENCE

Comecon Looks Ahead

from our Soviet Correspondent

THE new "complex programme" of economic integration of the COMECON countries, promulgated by the 25th session of COMECON, raises some interesting questions about the future of science and technology in eastern Europe. This programme, which will be implemented during the next 15–20 years, is aimed at the "further deepening and improvement of economic co-operation and the development of the socialist economic integration of the member countries of COMECON" by measures including a "collective currency policy", the sharing of research and development experience between the member countries, a common policy of external trade, and a coordinated plan for basic research and industry. This, however, is to be accomplished on a basis of "respect for national sovereignty, independence and national interests, non-interference in the internal affairs of member countries, complete equality of rights, mutual advantage and comradely cooperation". The programme will be based on "multilateral and bilateral mutual consultations", and will not be accompanied by the creation of new "supranational bodies".

This stress on national autonomy within COMECON seems to have been largely at the insistence of the Romanian delegation, which has been active in resisting what would appear to be the logical outcome of COMECON — virtual integration of the eastern bloc with the Soviet Union. But it seems unlikely that this view will stand up against the implicit supranational nature of the projects proposed by the programme. These include, in particular, the "planned expansion of international specialization and cooperation in industry, science and technology", the end result of which, whether decided by a supranational body, or by "direct links between the ministries and other state organs concerned", will be, to some extent, a curtailment of national autonomy as far as the choice of project is concerned.

A large section of the programme deals specifically with cooperation in science and technology. The emphasis here is on matters of policy, such as the planning and solution of important scientific and technical prob-

lems, cooperation in research and the interchange of information on research and development and mutual training programmes. The list of basic problems to be tackled using the "most effective forms of mutual cooperation" is long and somewhat vague in its terms, but seems to concentrate mainly on biology and biophysics, with special reference to agriculture and food production, mechanization, automation and computers, more efficient use of natural resources, including marine resources (the Pacific Ocean is especially mentioned, in a manner almost suggesting that it is a private preserve of COMECON), semi-conductors, and the demands of metallurgy and industry in general.

Much attention is given to the "organizational forms and legal principles" of the proposed cooperation, but no concrete projects are indicated. Information exchange is greatly emphasized, and, on the basis of the existing COMECON International Centre of Scientific and Technical Information in Moscow, a system of information exchange will be set up during 1972-73. The production of scientific instruments and apparatus will be one of the first fields to be reorganized and, during the next year, proposals are to be worked out by the member countries on the establishment of international societies for the production of high-precision instruments (including apparatus for nuclear research) and the establishment of a coordinating centre for cooperation on biomedical and clinical research equipment. Production of research materials is also to be integrated, including materials for optical spectroscopy, experimental physiology and high vacuum work.

Although the programme speaks throughout of the "member countries" and the "interested countries" involved in the various cooperative projects, it is inevitable that the Soviet Union will play the leading part in the planning. Although a COMECON scientific centre has sometimes been established outside the Soviet Union (Weed and Pest Control at Poznań, Timber Research at Bratislava), the location of the Information Centre in Moscow will tend to orientate all major planning towards Moscow.

EUROPEAN RESEARCH

Aigrain Projects Persist

PLANS have now been laid for a Pan-European conference on scientific and technical research in Brussels in November. The initiative comes from the Commission of the European Communities, and in particular from the technical working groups under Mr Pierre Aigrain which have in the past

two years sought to define the fields in which European countries might collaborate on scientific and technical projects. At a meeting in Brussels at the end of July, representatives of nineteen countries in Europe picked out a number of particular problems from the shopping list which has been accumulating since 1969. The intention is that there should be a conference in the second half of September to settle questions such as the organization and financing of joint research projects, and that the conference of ministers in November should then set up a series of specific collaborative projects on which work could begin immediately.

According to an announcement in Brussels, the original list of proposals has been narrowed down—a term which must be understood to include selection as well as refinement—to a number of specific issues. It has, for example, been decided that the most tangible way of making progress in collaborative data processing is to set up a European Data Transmission Network and then a program library. This, as it happens, is a project developed by the staff of the European Communities on the instructions of the Hague Conference on technical collaboration in September 1969. It is now proposed that the collaboration of European states should be invited in long-term studies of passenger transport, what are called "various means of combating nuisances", a term now understood to include not merely the properties of sulphur in the atmosphere but the treatment of mud and other solid waste. A newish departure is a series of projects in metallurgical research. There is talk of collaboration on radio wave propagation.

One striking property of the shopping list now current is the disappearance of some of the more ambitious projects such as the scheme for the development of a large computer. This, as it has turned out, is at once such a risky venture and one that promises such large commercial gain that the companies able to make a contribution to the project have preferred to get together among themselves and—prudently—to enlist American interest as well. Similarly, the original proposal for collaborative research in telecommunications is conspicuous by its absence—nobody pretends that Europe has too much good work of this kind, but it is clear that there are too many companies in Europe who think of themselves, perhaps with justice, as potential competitors of AT&T for collaboration to be easy at this stage. And, of course, from the beginning of these discussions about the future of European collaboration on technical developments, it has been assumed that, having burned its fingers with Euratom, the European

Community would not for the time being be able to turn its attention to fostering collaboration in the development of nuclear reactors. That is a stable door that nobody has the courage to shut even if the horse has not yet bolted.

HOVERCRAFT

How Fast for Hovertrain?

WITH the delivery this week from Vickers's Swindon factory of the first full-scale British tracked hovercraft, a new phase in the British development of this novel type of high speed surface travel is initiated. So far, the building programme of government-financed Tracked Hovercraft Limited (THL) at Cambridge has taken rather longer than scheduled for contractors to build a preliminary three miles of elevated box-beam track along the bank of a disused seventeenth century canal on the nearby Fens. In parallel, at the Cambridge laboratory, a variety of scale trials and studies of fundamental design features of the proposed vehicle have taken place, particularly concentrating on the specially developed single-sided linear electric motor for propulsion and the characteristics of the table-top sized hoverpads that will provide both lift and guidance.

The newly delivered 75 foot car is being equipped at a trackside workshop at the Erith terminal of the test monorail. All the interior equipment, the hoverpads and the linear motor installation are being handled by THL staff. The fitting out is expected to take some two months. The craft will then weigh 51 tons. Trials on track will then start. In view of the short length so far completed, the RTV3L vehicle is not intended to exceed 150 m.p.h. this year though rated for 300 m.p.h. (450 k.p.h.). The hope is to extend the track to five or eight miles next year when speeds up to 250 m.p.h. can be attempted. The craft will travel without a driver or passengers during the trials period. It is more efficient to control it electronically from the trackside and to use the interior space for every conceivable instrumentation so that no feature of "ride", vibration, acceleration, braking and so forth goes unrecorded.

There is one question to be answered: having received delivery of a 300 m.p.h. vehicle, is THL going to be able to exploit it? It seems to depend on a further subvention from government for extending the track to at least eight miles: eighteen were originally in view. The £3½ million initial investment is not yet exhausted, but by the end of 1971 the need of further investment will be becoming urgent. So far the government has studiously avoided committing itself in any way.

NEW WORLD

Metric Standards Round the Corner

THE National Bureau of Standards has predictably recommended that the United States should switch over to a metric system of measurement in the course of the next decade. In the report of the US Metric Study, which has occupied the bureau since the passing of the Metric Study Act by Congress in August 1968, the principal theme is that the metric system is for practical purposes unavoidable. "Eventually the United States will join the rest of the world in the use of the metric system as the predominant common language of measurement." But even the adoption of externally designed units of measurement may become a patriotic challenge. "Americans working cooperatively can resolve this question once and for all."

The report of the Metric Study has the inelegant title *A Metric America: A Decision whose Time has Come* (US Government Printing Office, \$2.50). The supporting evidence presented at the hearings of the study group has been published separately in twelve volumes. Responsibility for the study, originally placed with the Department of Commerce by Congress, has been delegated to the National Bureau of Standards but the Secretary of Commerce has also received advice from a large representative committee. Most of the evidence on which the report is based was collected during the summer of 1970 at public meetings which lasted altogether twenty days.

It remains to be seen what Congress will make of the report on metrication and of the argument that metrication is historically necessary. Congress failed to respond to Jefferson's commendation of the metric system as long ago as 1790, even before the definition of the metre. Since then, Congress has built up a long record of flirtation with bits and pieces of the metric system, especially at the turn of the century. Most recently, the United States seems to have been prodded into action partly by the National Bureau of Standards itself and partly by the spectacular example of countries such as Britain which have astonished not merely the tourists but themselves in their conversion to the metric cause.

The report of the study group says that the deliberate encouragement of the tendency towards metric could quite quickly create a situation in which the metric system was as widely used as the conventional system in the United States. Schools, it says, should emphasize metric measurements. Industries could be persuaded to conversion before they were forced by cir-

cumstances to measure metrically, and public authorities responsible for traffic signs and the like should seize their opportunities to make a captive audience think in kilometres.

In the same spirit of gradualism, and with some regrettable signs of falling for the confusion between units of measurement and standardization of sizes, the committee seeks to comfort anxious Americans by pointing out that it will never be necessary to change the size of an American football field or to alter the gauge of the great railroads (which may in any case be out of business before metric ways are adopted in the United States).

But what will the United States gain from such a development? The study group points out that agreements such as that between the United Kingdom, Germany and France on metric electronics arts, themselves the prototypes of more ambitious agreements yet to be negotiated, could exclude many American products from important markets. The study group has even calculated that American exports likely to be at risk in this sense in 1969 accounted for \$14,000 million and that an American failure to move towards the metric system will mean that something like \$600 million worth of exports will be unsold in 1975.

The Metric Study report points out that the compatibility of United States standards with those of other countries, particularly in Europe, may be particularly important at a time when the United States share of world trade is diminishing steadily—it fell by more than ten per cent during the sixties—and when arrangements such as the European Economic Community will provide further deterrents to American exports. Multi-national corporations are yet another source of pressure towards metrication.

The study group's enquiries among industrial companies seem fully to support its conclusions. In a sample of 4,000 companies chosen to represent American industry as a whole, those for the metric system represent a majority of the labour force, with larger companies more anxious to switch over. As a whole, 70 per cent of the labour force seems to be employed by manufacturers anxious to make the change. Among the general public, the study group's chief discovery seems to be that ignorance is the most common condition—only 40 per cent of the respondents to a social survey were able to name a single metric unit. In industry and among the public as a

whole, however, it seems to be accepted that if there is to be a change, it should be planned as a coordinated operation and spread over the next ten years.

With this starting point, the study group urges that there should be a coordinating organization to superintend the changeover. The study group has also singled out two points at which an early start could be made on adaptation to the future—closer participation in the making of international standards and the incorporation of metric measurements into school curricula. In the long run, there will have to be special studies of particular problems such as that already being undertaken by the Industrial Fasteners Institute on the definition of metric thread sizes. Eventually, there will also have to be some decisions about the extent to which collaboration between manufacturers on the development of metric standards can be freed from the threat of anti-trust prosecution. The study group has also committed itself to a complicated cost-benefit analysis of the transition to metric. It assumes, conservatively perhaps, that the benefit of an extra \$600 million a year on the balance of trade is more than \$1,000 million for the economy as a whole. Moreover, the study group points out that there would be a number of important economies arising from the way in which the transition to a metric system would provide opportunities for simplifying present practice and, for example, for reducing the numbers of standard items of equipment such as screw thread sizes. The cost of the transition, for manufacturing industry, is estimated to be between \$6,000 million and \$40,000 million spread over ten years. In general, therefore, the committee suggests that the costs are unlikely to be much greater than the benefits.

Whether the report now published will finally tip the scales in the United States in favour of conversion to metric may be an open question, but there is no doubt that the report will do a good deal for the moral of the Metrication Board in the United Kingdom, recently much cast down by the apparent indifference of the Conservative Government. Indeed, the working group declares that the British metrication programme should be regarded as a pilot for the conversion in the United States. Lord Ritchie-Calder, chairman of the Metrication Board, will no doubt be reminded once more that prophets are not highly regarded in their own countries.

NEWS AND VIEWS

The Universe Considered as Hole

DURING the past few years, astronomers have gained an insight into black holes (or collapsars) which has made the study of these phenomena an increasingly important part of astronomy. This field of research was once largely the preserve of mathematicians concerned with the nature of space-time in an abstract way; observational developments now suggest, however, that collapsars play a vital part in the evolution of stars, galaxies, and the Universe as a whole. The latest calculations pointing to the possible importance of collapsars in binary systems appear in this issue of *Nature* (page 465). G. W. Gibbons and S. W. Hawking have followed up the line of investigation pointed to by Trimble and Thorne (*Astrophys. J.*, **156**, 1013; 1969) and conclude, from a study of the properties of seven systems shown to be binary stars by the Doppler motion of lines in their spectra, that there is suggestive evidence for the presence of black holes in some binaries. This must also lend weight to the contention made by Cameron and supported by Stothers that there is a collapsar in the system ϵ Aurigae (*Nature*, **229**, 178 and 180; 1971).

But what exactly is a collapsar? The general scientific imagination may well be captured by this concept of a "hole in space", but all too often it is felt that, because the prediction of this effect stems from Einstein's general theory of relativity, an understanding of it requires specialized mathematical knowledge. This is far from the truth. Like many of the fruits of this elegant theory the prediction, once made, can easily be understood in physical terms. Any star with more than 1.4 solar masses left when it has exhausted its nuclear fuel cannot support itself against gravitational collapse. The pressure at the centre of the cold star becomes so great that the fundamental nuclear forces are overcome, and matter is compressed beyond the density of atomic nuclei. This process is self sustaining, because such compression results in a higher density, a stronger gravitational field, and thus still more rapid collapse. Eventually, the collapsar has the properties of a point source of infinitely dense material. Curious as this is, it is the effect of the gravitational field produced on the space outside the collapsar which is responsible for the current wave of interest in black holes.

Within a critical radius (the particle horizon), the field is so intense that no matter, nor any radiation, can escape from the collapsar, although material can continue to be absorbed from the Universe. Hence the name black hole—the only way in which these objects can be detected is by their gravitational fields. This has great appeal to cosmologists, many of whom believe that there should be more matter in the Universe than can be seen in the form of bright galaxies. It also opens the way to intriguing mathematical games concerned with the possibility of extracting energy from these sources.

The most extravagant suggestion is that matter swallowed up by black holes re-emerges into the Universe from white holes, which lie at the centres of active galaxies and quasars. This could ensure the overall conservation of mass/energy while offering some explanation of the extremely violent events observed in some astronomical

objects. At a more sophisticated level, it seems that energy could be extracted from the immediate vicinity of a collapsar by the break up of another object passing nearby. During a conference held from July 19 to 21 at the Institute of Theoretical Astronomy in Cambridge, which will shortly be reported in *Nature*, there was discussion of the properties of the ergosphere, a region just outside the particle horizon. A mass passing through this region can break up under certain conditions in such a way that one fragment falls into the black hole while the other is accelerated, gaining energy in the same way that the proposed grand tour space probes will gain energy from the rotational energy of the giant planets—a slingshot effect. But the escaping fragment can gain so much kinetic energy that it leaves the region of the collapsar with more mass/energy than that of the entire incident mass.

This mechanism must unfortunately remain a toy for the mathematicians, because the collapsars required to explain the activity of many observed galactic nuclei in terms of this effect would be implausibly large. For the present, however, practical astronomers and physicists would prefer to seek some other energizing process for these active galaxies and quasars. Black holes need not, however, be quite so extremely violent as this conventional picture conjures up. To be sure, objects like stars can only disappear inside their own particle horizons when compressed to very great densities. But while the mass of a sphere of matter at some uniform density varies as the cube of the sphere's radius, the gravitational force falls off only as r^2 . For any density chosen there is some critical mass above which the sphere is within its particle horizon, or, alternatively, for any mass there is some critical density for which this occurs, and the greater the mass chosen the smaller is the required critical density. So although gravity is a weak force, its action over very great distances implies that a reasonably dense galaxy—that is, one with a density comparable to the density of some stellar clusters in our galaxy—could contain enough mass to prevent the escape of matter or radiation from its immediate vicinity.

Once again, the cosmologists who wish for more matter in the Universe are delighted—now, it seems, whole galaxies can be hidden in black holes. But why do the cosmologists want yet more matter in the visible galaxies? In short, it is to provide enough mass for the Universe to be closed. This would solve many problems regarding the nature and origin of the Universe, and would fit many of the observations of distant sources made at radio, optical and other wavelengths. But if the Universe is closed—the finite, yet unbounded three-dimensional analogue of the surface of a sphere—then the world is in essentially a rather large black hole. The corollary to this is that the expansion of the Universe must ultimately be reversed, eventually producing a compression to densities where present understanding of physics breaks down, with, perhaps, a further expansion from the primaeval matter in a cycle of pulsations which had no beginning and will have no end.

Significance of Sex Linked Antigens

THE observation that individuals of the same species may differ from each other antigenically is now so well established as to hardly bear remarking. Antigen hunting, the identification of more and more antigens, has rightly fallen into disrepute as a worthwhile activity, yet it cannot be claimed that there is any clear idea of the biological significance of the remarkable antigenic variation observed in most mammalian species.

Two extreme views for this variation can be put forward. The first is that it arises as a result of a random event, mutation, but that one form of the antigenic material confers some kind of biological advantage, and the alternative form confers another kind of advantage. Antigenic variation, as pointed out by E. B. Ford, would thus form an example of a balanced polymorphism, and takes its place with such phenomena as variation in rings on snail shells and spots on insect wings as part of a more or less homogeneous group of biological variations. On this hypothesis there is a need to look only for a cause for the maintenance of the antigenic variation, and it may be fortuitous that the variant materials are antigenic. They have a role in the cell membrane, and one antigenic form may be more advantageous in one environment than in another.

The alternative hypothesis is that it is the antigenicity of the materials which is important. There have been many hypotheses that have utilized this idea—one of the most recent is the suggestion of Jerne (*Europ. J. Immunol.*, 1, 1; 1971) that histocompatibility antigens, such as H-2 antigens in the mouse, may play a part in the generation of immunoglobulin diversity. It has also been frequently suggested that histocompatibility antigens play a part in distinguishing neoplastic cells from normal cells, although the way in which this is done is far from clear.

These two kinds of hypothesis can, of course, be merged into one, because all variation must originate in mutation, and it can hardly be the case, for example, that the need to distinguish neoplastic and normal cells gave rise to antigenic variation—the origin of any variation must precede its utilization.

Even if this view of the origin of variation is accepted, it is still necessary to look for the reason for its survival, that is, for its "function". The direct demonstration of the mouse H-Y antigen, controlled by a gene on the Y chromosome, on mouse spermatozoa by Goldberg, Boyse, Bennett, Scheid and Carswell (see page 478 of this issue of *Nature*) puts this antigen firmly on the map as an antigenic system the biological role of which ought to be investigated. The use of skin grafts to investigate the H-Y antigen has hitherto clearly limited what could be done.

If it is acknowledged that antigen systems like H-Y in the mouse, and the human Xg^a blood group antigen (controlled by an X chromosome gene), may have biological roles, why are the genes that control them on the X or Y chromosomes? The same question can, of course, be asked of other genes present in moderately high frequency in the population, such as those on the human X chromosome which affect colour vision. One should not, perhaps, make too much of this—the X and Y chromosomes represent a considerable proportion of the animal's genetic material; that it can all be concerned with sexual differentiation seems unlikely.

Apart from these rather vague speculations, it is much easier to comment on the usefulness of these antigens to investigators. Race and Sanger, in their book *Blood Groups in Man* (Blackwell, Oxford and Edinburgh, 1968), point out how the investigation of the Xg^a blood group has revolutionized knowledge of the human X chromosome linkage group, and indeed of human genetics as a whole. The development of a direct cytotoxic test for the mouse H-Y antigen by Goldberg *et al.* could do the same for the mouse. Although many of the investigational problems which beset human genetics do not exist in the mouse, the development of a serological test will be a great spur to the investigation of the mouse Y linkage group, and it might one day lead to an answer to the question posed earlier—whether or not the H-Y gene is present on the Y chromosome fortuitously.

It is worthwhile drawing attention to another specific feature of Goldberg's work, that at least some, and

therefore possibly all, X bearing spermatozoa carry the Y antigen and thus reflect the antigenic constitution of their precursor cells rather than the capabilities of the genetic material contained in the sperm; similar observations have now been made on several antigenic systems in spermatozoa. This therefore precludes the use of an immunological method, with any antigen system so far discovered, of either distinguishing or separating X or Y bearing spermatozoa, and is unlikely to form the basis of a technique for deliberate selection of male or female offspring.

DNA REPLICATION

Selective Inhibition

from our Cell Biology Correspondent

THE substituted uracil derivative, 6(p-hydroxyphenylazo)-uracil (HPUra) is today unlikely to be found outside the laboratory of N. C. Brown in Baltimore, who since 1966 has diligently been investigating its effects on DNA synthesis and DNA replication in a variety of bacteria. But to judge from what he has to say in the *Journal of Molecular Biology* (59, 1; 1971), the manufacturers of this compound, Imperial Chemical Industries Limited, can anticipate a spate of begging letters. For, according to Brown, HPUra inhibits the semiconservative replication of DNA without affecting DNA repair.

During the past five years Brown has shown that although the compound selectively and reversibly inhibits DNA replication in *Bacillus subtilis* and a range of Gram positive bacteria it does not bind with great affinity to DNA, it does not stop the replication of phage in *B. subtilis*, neither does it impair transcription, translation or the synthesis of bacterial cell wall materials. Attempts to characterize the way in which the drug acts by adding it to a range of membrane fractions, preparations of *B. subtilis* exposed to lysozyme and apparently even cells made permeable by exposure to toluene, have all failed. The DNA synthesis which these systems support *in vitro*, like the replication of phage (Brown, *Proc. US Nat. Acad. Sci.*, 67, 1454; 1971), is refractory to HPUra.

Because of this Brown was forced to re-examine the effects of this compound on intact bacteria because they alone support the DNA replication process sensitive to HPUra. He selected the strain of *B. subtilis* 168 *thy⁻ ind⁻* for this work, for as Pettijohn and Hana-

walt have shown, cells of this strain, after exposure to ultraviolet irradiation, support extensive DNA repair synthesis and they therefore offer an opportunity of comparing the effects of HPURa on repair and replication. In an elegant series of experiments Brown has shown that although the semiconservative replication of the chromosome of this strain is blocked by HPURa, the repair of DNA damage caused by the ultraviolet irradiation continues unabated. For example, he labelled the DNA made after irradiation and in the presence of the drug with radioactive bromo-deoxyuridine and then analysed it on caesium chloride and alkaline gradients. The bulk of the labelled DNA turned up in short chains covalently linked to the parental DNA. Moreover the synthesis of this DNA was greatest in cells given the highest doses of irradiation, and it was inhibited by inhibitors of excision repair synthesis such as actinomycin D.

Because Brown found last year that the replication of virulent phages in *B. subtilis* is not blocked by HPURa he was at pains to eliminate the possibility that the synthesis of DNA in irradiated cells, which is insensitive to HPURa, is nothing more than the replication of a defective prophage induced by the irradiation. The properties of defective *B. subtilis* prophages make this idea implausible and furthermore he has shown, first, that synthesis of DNA in irradiated cells does not immediately depend on protein synthesis and, second, that mitomycin C treatment, which like irradiation induces defective prophages of *B. subtilis*, does not induce an HPURa-refractory DNA synthesis. In short, there seems little doubt that it is the repair of irradiation damage that continues in the presence of HPURa.

If HPURa is as selective an inhibitor of DNA semiconservative replication as Brown's work indicates it should prove an extremely useful tool for identifying the real DNA replicase. But Brown's claim that DNA synthesis in toluenized cells continues in the presence of this drug (and unfortunately he has not yet published the detailed evidence on which he rests this assertion) must come as a blow to cell biologists who have pinned their hopes on toluenized cells as a system for investigating DNA replication *in vitro*. The experiments reported by Sueoka's group in *Nature New Biology* (232, 111; 1971), for example, certainly suggest that toluenized *B. subtilis* cells support DNA replication rather than repair synthesis, but Brown's findings raise new doubts about that. If Brown is right, toluenized cells may have to be added to the scrap heap of bacterial preparations which, although they make DNA *in vitro*, do not support chromosomal replication identical to that occurring in intact cells.

ANTIQUITIES

Fooling the Experts

from our Archaeology Correspondent

NEW thermoluminescence work on supposedly ancient ceramic objects, all recently acquired by museums and collectors, shows how successfully forgers and fakers are taking in their clients. Two studies undertaken at the Research Laboratory for Archaeology and the History of Art at the University of Oxford indicate not only the effectiveness of the thermoluminescence method, but the great difficulty that experts have in distinguishing genuine objects from false ones simply by their appearance.

The first study, by M. J. Aitken, P. R. S. Moorey and P. J. Ucko (*Archaeometry*, 13, 89; 1971), exposes as fakes no fewer than forty-eight out of sixty-six bowls, figurines and anthropomorphic vessels, which have supposedly come from illicit excavations at the prehistoric site of Hacilar in Turkey. Since the successful excavations there by James

Mellaart in 1957 and subsequent years (*Excavations at Hacilar*, I and II: Edinburgh Univ. Press; 1970), the attractively painted pottery and baked clay figurines discovered have rightly had an important place in the early history of art. Similar objects from illicit excavations have fetched up to £3,000 on the antiquities market.

Thermoluminescence glow curves obtained by Aitken show that most of the specimens examined emitted very little light on heating. The thermoluminescence observed is proportional to the radiation which the clay has undergone since it was fired—the radiation originates chiefly from radioactive isotopes in the clay or in the soil in which the object was buried—and hence upon its age since firing. Forty-eight out of sixty-six objects were evidently recently fired. The remote possibility that genuine ancient pieces had undergone heating in recent times to consolidate them, thereby removing the accumulated thermoluminescence, was checked by S. J. Fleming and D. Stone-

Streptovaricins Suppress Oncogenicity

LAST March Brockman and his colleagues reported in *Nature* (230, 249; 1971) that the streptovaricins—a family of antibiotics, the structure of which is similar to that of the rifamycins—inhibit the activity of reverse transcriptase in mouse leukaemia virus particles. At concentrations of 40 µg/ml. the enzyme's activity was inhibited by 75 per cent. In next Wednesday's *Nature New Biology* Brockman's group describe their latest experiments with these drugs which show that streptovaricins not only inhibit the transformation by mouse sarcoma virus of mouse 3T3 cells growing in culture, but also selectively inhibit the progress of erythroblastic leukaemia and spleen enlargement induced in mice by Rauscher leukaemia virus. Their work thus suggests that streptovaricins might become useful chemotherapeutic agents for the treatment of cancer.

At concentrations which do not slow down the rate of cell division, those streptovaricins which inhibit reverse transcriptase also block by from 25 to 50 per cent the induction of foci of transformed cells by mouse sarcoma virus. This fact, together with the finding that the antibiotics are ineffective 24 h after infection, suggests that the inhibition of transformation results from the inhibition of reverse transcriptase activity. Moreover the inhibition of transformation by streptovaricins was enhanced if the cells were exposed simultaneously to interferon, which Brockman *et al.* suggest specifically inhibits the translation of viral messenger RNAs.

But inhibiting transformation *in vitro*

is one thing; inhibiting the induction of a cancer in an intact animal is another. Can streptovaricin alter the course of events after mice are infected with a virus such as Rauscher leukaemia virus? According to Brockman and his colleagues it can. They find that mice fed streptovaricin in their food such that the concentration of the drug in their serum is from 1 to 3 µg/ml. are protected to a significant extent against splenomegaly induced by Rauscher murine leukaemia virus. The spleens of mice fed the drug before and throughout the infection are only about 50 per cent as large as those of mice given the virus but not the drug. Moreover when the drug is not given until 8 days after infection, when spleen enlargement is well under way, it can still significantly reduce further enlargement.

These findings, together with the observation that streptovaricin does not inhibit transformation *in vitro* if it is given 24 h after infection, lead Brockman's group to conclude that *in vivo* the drug is blocking secondary focus formation in the spleen. The drug does not, however, reduce the proliferation of normal haematopoietic cells, as judged by spleen focus counts, neither does it impair spleen enlargement in mice inoculated with the L1210 transplantable lymphoma cells.

In short, in mice the streptovaricins seem to block a virus-induced oncogenic event rather than affecting the proliferation of malignant cells. In the intact animal it may therefore be acting as an inhibitor of tumour virus reverse transcriptase.

ham. They used the "pre-dose" technique, which depends on the enhanced susceptibility, after heating, to artificial irradiation shown by specimens which have previously had a radiation dose. Most of the samples with negligible initial thermoluminescence showed a small increase in susceptibility to irradiation after simulated re-firing, which suggests that they never had experienced the appreciable dose of radiation received over 7,000 years, in the normal course of things, by the genuine antiquities.

The second investigation, by S. J. Fleming, H. Jucker and J. Reiderer (*ibid.*, 13, 143; 1971), reveals that most or all of the Etruscan wall paintings on terracotta recently on the Swiss and American art markets are very palpable fakes. The museums owning these painted slabs will have paid anything up to £10,000 each for them. Fleming *et al.* used both the fine grain and the inclusion thermoluminescence methods—the inclusion method utilizes the large quartz and other mineral grains present as inclusions in the clay—and a comparison of the results shows that the painted plaques were made some time during the past twelve years.

The layman, of course, always derives a little innocent pleasure from seeing the experts fooled—a pleasure which will not be shared by the museums in Bern, Basel and Munich owning "Etruscan" terracottas, or by the custodians of the Hacilar material around the world. A more serious consequence of such faking activities is brought out in Ucko's discussion. The fakes include a number of variants and ostensibly new types accepted, until now, as genuine by most authorities. Indeed the abundance of new "finds" on the market led Mellaart to propose that looters had discovered the hitherto unknown cemetery at Hacilar, unearthing vases which "probably were used only in ritual functions in shrines and graves". Ucko now suggests that the few genuine pieces could all have come from illicit digging in the settlement itself, so that the whole interpretation of the meaning and function of such genuine pieces as remain becomes very different.

It is a sobering thought too that, for most materials other than baked clay, no method as reliable as thermoluminescence exists for detecting fakes. Luristan bronzes and Cycladic marble figurines are but two more of the fields where collectors and museums have been consistently and profitably defrauded. There are far more of them in the museums of the world than ever were excavated. The obvious moral is that museums should be less eager to encourage illicit excavation by paying large sums for unprovenanced antiquities. By doing so they are supporting, often very generously, looters and fakers alike.

BEHAVIOUR

Displays Analysed

from our Animal Behaviour Correspondent

THE most striking aspects of an animal's behavioural repertoire are often the "displays" it gives in sexual or aggressive encounters. Much is now known about the behaviours which birds and fish show during courtship and aggression, and there has been much speculation as to the underlying physiological mechanisms which give rise to these conspicuous displays. Elements of displays of animals, and sometimes whole behavioural sequences, can now be produced by electrical stimulation of the brain or by injection of hormones. The idea that such displays might be a particularly fruitful meeting ground for ethology and

physiology prompted the meeting of the Association for the Study of Animal Behaviour at the University of Sussex from July 26 to 29. As Professor R. J. Andrew (University of Sussex) pointed out, displays have been selected during evolution to provide an accurate "read out" of an animal's internal state to another animal, and so may well be able to do so for the human observer.

The meeting provided an excellent opportunity for the exchange of ideas, but it soon became clear that there is still a long way to go before the physiology of even the most commonly observed displays is elucidated. There were several reports of researches into the role of various brain structures in controlling behaviour, but the precise function of these areas and their inter-relations with other parts of the brain are still obscure, possibly because the

Exploding Magnetosphere May Cause Crab Glitches

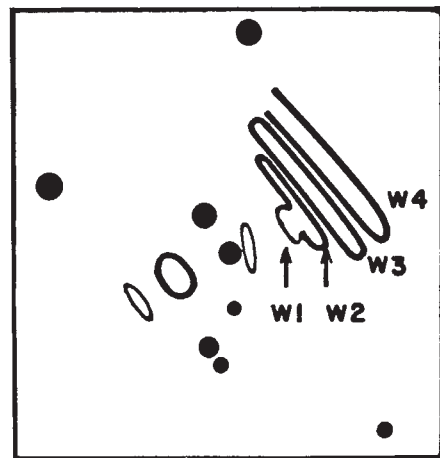
BEFORE detailed timings of the Crab pulsar became available, astronomers were concerned to explain the amazing regularity of pulsar pulses. But now it is the small irregularities that have been revealed in the periodicity of the Crab pulsar for which explanations are being sought, in terms of the view that pulsars are rapidly spinning neutron stars which provides a satisfactory explanation of the gross features of pulsars. A review of the considerable data now available on the irregularities of the Crab pulsar—the largest and most sudden of which are called glitches, although an entire spectrum of events of different magnitudes and time scales can occur—is given by Jeffrey Scargle of Lick Observatory and Franco Pacini of the Laboratorio di Astrofisica at Frascati (Italy) in next Monday's *Nature Physical Science*.

The popular view that the irregularities are caused by what are called "starquakes" in a solid outer crust surrounding the neutron superfluid core of a neutron star does not find favour with Scargle and Pacini. Although changes in the internal structure of a neutron star, such as a starquake, would lead to an alteration in the moment of inertia of the spinning star that would be reflected in a change in the periodicity of the pulses, Scargle and Pacini point out that this notion is unsatisfactory on energy considerations.

The reason is that some filamentary concentrations of gas adjacent to the Crab pulsar seem to move in tune with the glitches, requiring more energy than can be provided by the starquake explanation. As an alternative explanation Scargle and Pacini suggest that the gas is excited from time to time by the sudden release of plasma from the magnetosphere of the pulsar, which

would also lead to changes in the dynamics of the spinning pulsar that would be reflected in the pulse periodicity.

These occasional outbursts supplement the continuous injection of energy into the Crab Nebula by the escape of particles from the pulsar along open field lines. Much work needs to be done to investigate the kinds of plasma instabilities that can occur in the magnetospheres of neutron stars, but on the face of it this model seems to be a neat way of accounting for several features of the Crab pulsar.



The Crab pulsar, at the centre of this diagram, seems to be associated with a series of wisps of gas, W1, W2, W3 and W4. According to the review by Scargle and Pacini, Wisps 4, 3 and 2 seem to have been generated from Wisp 1, possibly as a result of the activation of Wisp 1 by the explosive release of plasma from the magnetosphere of the pulsar. The impact of this plasma pushes Wisp 1 out from the pulsar until the pressure is balanced by the pressure of the plasma and magnetic field of the Crab Nebula. Wisps 2, 3 and 4 have been generated by the magnetosonic waves which this motion of Wisp 1 produces.

brain, like a computer, can be "programmed" to do different jobs at different times. Indeed, the animal-computer analogy was heard more than once, from Dr J. D. Delius (University of Durham) and also from Dr D. J. McFarland (University of Oxford) who argued that animals allocate their time between different behaviours by "time sharing".

Physiological interpretation of a behaviour pattern is facilitated by an accurate description of the phenomenon to be explained, so that methods of recording and analysing behaviour are extremely important. Dr U. Weidmann (University of Leicester) illustrated his technique of frame-by-frame film analysis of the displays of mallard ducks as a method of discovering spatial and temporal relations between the birds that would be impossible by more conventional means. Dr P. Slater (University of Sussex) talked of the difficulties of describing and making sense of complex sequences of behaviour, and Drs R. Dawkins and M. Dawkins (University of Oxford) presented some methods of describing and predicting moment to moment changes in the fine structure of a behavioural act.

Better methods of description and the application of statistical techniques to uncover underlying patterns may well prove as useful a method for gaining an understanding of what goes on inside an animal as the already fruitful physiological approaches.

PROTEINS

Oxidation to Order

from our Molecular Biology Correspondent
A GROUP at the University of Padua, Jori, Scoffone and their colleagues, have cornered the market in photo-oxidation of proteins. By a series of chemical subterfuges they have shown how the scope and precision of the method can be extended to make it potentially one of the most useful resources of the protein chemist. In their latest article (on papain) they present a striking demonstration of the delicate molecular surgery that is now feasible (Jori *et al.*, *J. Mol. Biol.*, **59**, 151; 1971).

Papain contains a single thiol group, which is a part of the active site, and is readily modified. A suitable chromophoric group attached to it can then be used as a sensitizer for the photo-oxidation of reactive side chains in the immediate vicinity. Jori and his colleagues examined two such sensitizers—the dinitrophenyl and the fluorescein thiocarbonyl groups. Their insertion caused no disturbance in the structure of the protein, as reflected in its optical properties. The dinitrophenyl group gave rise to its own Cotton effect in circular dichroism, indicating that it

was rather rigidly set in its place in the protein. The fluorescein chromophore on the other hand showed no such effect, and from its low fluorescence polarization it could be inferred that there was little restraint on its rotation.

It might consequently be supposed that with its less restricted orientation it might function as a less discriminating photosensitizer. This expectation is borne out: the dinitrophenyl chromophore permits the destruction of only two residues, which were identified by separation of tryptic peptides as a histidine and a tryptophan. The fluorescein chromophore sensitizes the oxidation of both of these and also of a further tryptophan in the early stages of irradiation, and then increasingly indiscriminate destruction of residues in all parts of the chain. If the protein is denatured before irradiation, the side chains in the dinitrophenyl derivative are also extensively oxidized on irradiation.

From the papain structure, and indeed from what is known of its chemistry, the two residues destroyed in the native dinitrophenyl derivative are known to be in the active site, and no more than about 5 Å from the substituted cysteine. The protein so modified retains its native conformation, with unimpaired thermal stability. The second tryptophan initially modified in the fluorescein derivative is not in the active site, but is tucked into a tight-packed internal region close by. When this residue is oxidized, previously inaccessible groups become exposed, the optical properties change, and all the indications are that the tertiary structure has broken down. The conclusion is that the tryptophan in question is indispensable for maintaining the integrity of the conformation of the native enzyme.

A further refinement to the photo-

oxidative approach has been evolved in the same laboratory (Jori *et al.*, *Biochim. Biophys. Acta*, **236**, 746; 1971). It is well known that paramagnetic ions are efficient quenchers of electronically excited states, and presumably for this reason are able to afford protection against photo-oxidative damage. The possibility then arises of making use of specific binding of such ions by proteins to achieve selective protection of some of the side chains which would otherwise be destroyed in a sensitized photo-oxidation process. Lysozyme is known to have a single strong binding site for zinc or cobalt. The site is known from protein magnetic resonance studies to consist of the carboxylate groups of glu-35 and asp-52. When the zinc complex is irradiated in the presence of proflavine as photosensitizer, tryptophan and methionine side chains are annihilated and the enzymatic activity vanishes. If on the other hand the paramagnetic cobalt ion is substituted for zinc the activity after irradiation does not fall below 85 per cent of native, and two indole rings are found to have been degraded. These are external side chains (trp-63 and 123), and do not perceptibly affect the conformation of the protein.

Experiments with ribonuclease gave similar results: the free enzyme or its zinc complex were extensively damaged but the cupric complex was modified only at two residues, met-79 and his-105, with substantial retention of activity. This result answers finally the question of whether met-79 is implicated in the enzyme mechanism. The protective effect of the paramagnetic ion is clearly a function of distance and orientation, and the possibility exists of exerting a finer control on the reaction by the choice of metal ions with different orientations of ligand orbitals.

Accurate Radio Source Positions from Cambridge

AS the relationship between radio, optical and high energy emission from sources both inside our galaxy and from extragalactic sources is becoming increasingly important to an understanding of the processes operating in these objects, so it is of increasing importance that radio sources should be pinned down by accurate measurements of their positions. Without the painstaking work which this implies, no correlation can be made between radio sources and optical objects. Equally important is the establishment of an absolute reference scale, so that positions determined using different antennae can be adequately compared. In next Monday's *Nature Physical Science* J. W. Smith reports the latest progress made in this field by the team operating

the Cambridge One Mile radiotelescope.

By carrying out simultaneous observations at 2.7 and 5 GHz, corrections allowing for the curvature of the atmosphere, and seasonal variations in the electrical lengths of the delay cables in the equipment are included—these terms are as small as 0.01 arc s. The overall accuracy of the positions given by Smith for twenty-eight sources is not, of course, as accurate as 0.01 arc s. But the better than 0.05 arc s accuracy quoted for right ascension, and better than 1 arc s for declination, is already pressing the optical astronomers, who will now need to improve their own measurements before a deeper insight into these sources can be achieved.

THE EARTH

Chondritic After All?

from our Geomagnetism Correspondent

THE chemical nature of the Earth's outer core has been a source of speculation ever since seismological evidence proved unequivocally that this part of the Earth is fluid. It is now completely accepted that the principal element in the core is iron although Earth scientists are rather less inclined to speculate upon to what extent such iron may resemble conventional molten iron under the conditions of temperature and pressure which obtain in the core. But this problem apart, the principal area of disagreement remains the content of the core's minor element. For various reasons the prime contenders here are nickel and silicon; but Murthy and Hall (*Phys. Earth Planet. Interiors*, **2**, 276; 1970) have suggested that the most important minor element may be sulphur.

It has long been known that where hydrated minerals (for example, hydrous silicates) are present, the low-temperature accretion of an Earth which is roughly chondritic requires the retention of sulphur as FeS under all conditions of temperature and pressure and thus requires the relative solar proportion of sulphur in the Earth as a whole. Various considerations thus led Murthy and Hall to argue that the first melt to form during the early history of the Earth was an FeS-Fe eutectic which would have effectively transferred chalcophilic elements from the lithosphere to the core, that a core with 15 per cent sulphur would have a density lower than that of any Fe-Ni alloy and would thus be more in line with many seismological estimates, that thermal models of the Earth which take account of the presence of FeS indicate earlier core formation than other models, and that to have had early core formation and differentiation of the Earth would have required neither high accretion temperatures nor a basic difference in chemistry between chondrites and the proto-Earth. There are, nevertheless, serious objections to a chondritic Earth in the first place, one of the most important of which is that the alkali metals, potassium, rubidium and caesium, are several times less abundant in the lithosphere than differentiation of a chondritic Earth would indicate.

Taking up the matter where Murthy and Hall left off, Lewis (*Earth Planet. Sci. Lett.*, **11**, 130; 1971) now argues that the presence of sulphur in the core removes many of the apparent discrepancies between the real Earth and the chondritic Earth. His basic thesis is that, contrary to popular supposition, the three "missing" elements, among others, have "appreciable chalcophilic tendencies" and that as a result their

depletion in the lithosphere is balanced by their enrichment in a sulphur-bearing core. In other words, the relative lack of abundance of these elements in the lithosphere should not be extrapolated downwards and thus does not necessarily imply that the Earth cannot be chondritic as a whole.

Needless to say, there is little direct evidence for this, but Lewis can nevertheless point to certain factors which support his case. Thus although the oxide-sulphide equilibrium is not relevant, as such, to any process occurring in the interior of the Earth, equilibrium constants show clearly that the alkali and alkali metal sulphides are extremely stable with respect to the corresponding oxides—a fact which Lewis believes to be indicative if not definitive. Second, in ordinary chondrites the alkali metals are almost always present in the silicate minerals and not in oxides, sulphides or oxy-salts. A consideration of the reactions of Mg_2SiO_4 and $CaSiO_3$ with FeS in relation to olivine at a temperature of 240° C above the FeS-Fe eutectic then indicates that small amounts of CaS and MgS are stable relative to FeS and thus are likely to enter an FeS-Fe melt even

with silicates in the same state of oxidation as in the present mantle. Moreover, CaS and MgS have been found in many enstatite chondrites and achondritic meteorites; and some of such enstatite chondrites also contain sulphide phases containing Na, K and Ti. In Lewis's view there seems no reason to suppose that where K goes Rb and Cs should not also follow, especially because the equilibrium constants for these elements in the oxide-sulphide reaction are very similar.

The difficulty in proving Lewis's point lies largely in the lack of thermodynamic data on the behaviour of the relevant sulphides in FeS-rich melts; and matters are not helped by the almost complete absence of alkali metal sulphides in terrestrial rocks known to geologists. But in spite of the latter deficiency and the admitted difficulty of forming solid sulphides of Mg, Ca, K, Ti and Na, the impossibility of producing an FeS-rich melt with, say, a one per cent content of such sulphides is by no means clear. Indeed, the circumstantial evidence for such a mixture in the core is quite strong.

Lewis rightly points out that if the Earth's fluid core really is enriched in

Growth Regulation in Normal and Transformed Cells

IT is classic observation that mouse fibroblasts (3T3) cells stop growing when they reach confluence or when they are deprived of serum, whereas the same cells transformed by the oncogenic virus SV40 continue to divide. This system would seem ideal for gaining insight into the normal regulation of cell growth and the genesis of cancer, and consequently much information has accumulated about biochemical changes in the cells after transformation or during growth limitation. In next Wednesday's *Nature New Biology*, Hershko *et al.* extend these observations, and, grasping the whole nettle boldly by the hand, propose a unifying theory of growth regulation in animal cells and its disruption by tumour viruses.

They show that depriving untransformed, but not SV40 transformed, 3T3 cells of serum produces a marked inhibition of protein and RNA (particularly ribosomal RNA) synthesis, a reduction in the uptake of certain nucleic acid precursors and a stimulation of protein degradation. They argue that each of these diverse metabolic reactions is, independently, part of a coordinated programme, or "pleiotypic response", of normal cells to changes in growth conditions. The response may be "negative" or "positive" depending on whether growth is limited or stimulated. Considering the possible mechanism of the pleiotypic

response, Hershko *et al.* show that all the changes elicited by serum deprivation are reversed by insulin, even when bound to 'Sephacrose' and unable to enter the cell. This suggests that the pleiotypic response may be coordinated by an intracellular "mediator" generated at the cell membrane, much in the same way that cAMP brings about the diverse responses of tissues to activators of adenylate cyclase.

In support of their idea that several aspects of cell function are coordinated by a single, underlying mechanism, Hershko *et al.* draw a striking analogy between the negative pleiotypic response in animal cells and the "stringent" response in bacteria starved of essential amino-acids. The stringent response, controlled by a single *Rel* gene, was originally thought to affect only ribosomal and tRNA synthesis, but it now seems that other processes are involved, including the uptake and phosphorylation of certain nucleic acid precursors and glucose, the formation of polyribosomes and the degradation of protein, which are all elements of the pleiotypic response. For the present, however, the case for the defence must rest there, for the nucleotide ppGpp, implicated in the mechanism of the stringent response, does not seem to be present in normal, growth-limited, animal cells, and is therefore unlikely to be the postulated negative pleiotypic mediator.

K, Rb and Cs the consequences are at once numerous and far reaching. First, the relative depletion of the three elements in the lithosphere becomes immediately explicable; and the terrestrial abundances of the major elements become compatible with a chondritic source. Second, it is no longer necessary to invoke volatilization during high temperature accretion to account for the apparent disappearance of terrestrial potassium and sulphur. Third, it may no longer be necessarily true that the chondritic Earth model, which explains the observed terrestrial heat flow so well, is not valid simply because the crust and mantle do not contain enough K, U and Th. Fourth, as much as seven eighths of the ^{40}K in the Earth may be in the core, thereby forming a major heat source of about 10^{30} ergs s^{-1} . Even if the efficiency of conversion is only 10^{-4} there would be enough energy here to maintain the convection to produce the geomagnetic field.

The fifth point is that the rough equality of oceanic and continental heat flow, notwithstanding the greater concentration of radioactive heat-producing minerals in the continental crust, may be explained by convective upwelling of deep ^{40}K beneath the oceans. Sixth, the low abundance of ^{40}Ar in the atmosphere compared with the abundance to be expected from the decay of ^{40}K in a completely degassed chondritic Earth could be related to the impossibility of degassing radiogenic ^{40}Ar from the core. And, finally, the low abundance of ^{87}Sr in the crust may be the result of the removal to the core of much of the Rb early in the Earth's evolution.

But can so many consequences, covering, as they do, such a wide range of geophysical and geochemical problems, really stem from such a simple premise? It is possible, of course, that Lewis has underestimated the complexity of some of the problems his basic thesis purports to solve. Even so, his wide-ranging conclusions must surely force a re-evaluation of the problems which have turned most scientists away from the simple chondritic Earth.

PESTICIDES

Leaching from Soil

from a Correspondent

It is well known that fish and other aquatic organisms may concentrate organochlorine pesticides from very low levels in the water in which they swim until the amounts in their bodies are either lethal or too high for the fish to be eaten by man, so that this form of environmental contamination has received considerable study. The 1970 report of the Agricultural Research Council's Research Committee on Toxic

Chemicals showed that some organochlorine pesticides were likely to come from rainfall, but that factory effluents and accidents such as spills of sheep dip were more important. Measurable amounts of pesticides are washed off the surface of treated fields especially by flash floods, but "underground water, which has percolated through soil, has not been found to contain measurable quantities of organochlorines".

This conclusion is based on many observations, mostly in temperate countries. The British Ministry of Agriculture suffered some criticism for suggesting that the best way of disposing of surplus and unwanted DDT, shortly to be banned for use in gardens in Britain following the recommendations of the Advisory Committee on Pesticides and Other Toxic Chemicals (the Wilson Committee), was to rotovate it into the soil, though this is, in Britain, a method which is likely to localize the insecticide's effects, and is far safer than such methods as disposal down the drain, or bulk burial.

A disquieting report from Pakistan is contained in an article by Aslam I. Nasim, M. M. H. Baig and K. A. Lord, of the Toxicology and Pesticide Laboratory, Karachi (*Envir. Poll.*, **2**, 1; 1971).

These authors have found that organochlorine insecticides are widely distributed in soils in East Pakistan and are extracted by water from the soil. Nasim *et al.* examined six soil samples from three different localities near Dacca by silica-loaded paper and gas chromatography and found that all were contaminated with organochlorine insecticides and contained 1 to 3 p.p.m. of DDT. Furthermore, three of the samples contained 0.1 to 0.5 p.p.m. gamma BHC and three others about 0.5 p.p.m. dieldrin. BHC has been used in the past in Pakistan for the control of rice pests and dieldrin is used in the treatment of bamboo, but there seems to be no easy explanation for the DDT contamination.

Because insecticides are leached from soil by water, the presence of 1 to 3 p.p.m. of DDT and other insecticides in the soils examined by Nasim *et al.* could pose a threat to the fish life inhabiting paddy fields as well as the more direct contamination of water sources. Nasim *et al.* consider it essential therefore that further monitoring continues—freshwater fish are important sources of protein for the population of East Pakistan, and any deleterious effects of the insecticides on the fish populations could be serious.

Hormone-responsive Tumours

A FAVOURITE pastime of steroid endocrinologists in recent months has been hunt-the-receptor-protein, and attention is now turning towards the determination of the physiological relevance of these proteins. One aspect of this concerns their role in steroid-controlled growth of certain tumours. In general, hormone responsive tumours show a progression from a responsive to an unresponsive state, and this is associated with a loss or diminution of specific steroid-binding capacity (King, Smith and Steggle, *Steroidologia*, **1**, 73; 1970).

In next Wednesday's *Nature New Biology*, Kirkpatrick, Milholland and Rosen report a decreased amount of corticosteroid receptor in unresponsive P1798 lymphosarcoma as compared with the corticosteroid-responsive line. This confirms the earlier work of Hollander and Chiu (*Biochem. Biophys. Res. Commun.*, **25**, 291; 1966), but Kirkpatrick and his colleagues have taken advantage of a factor not usually available in this type of work, that a parallel biochemical response (DNA synthesis and membrane permeability) can be measured as an indication of the relevance of the steroid protein interaction. They also show that, contrary to one of the current vogues of cancer research, changes in the cell membrane cannot explain their results.

An unanswered question is what or where is the primary lesion causing this loss? Recent reports indicate that steroid specificity is controlled at the nuclear level as well as by the presence of a cytoplasmic protein (Steggles, Spelsberg, Glasser and O'Malley, *Proc. US Nat. Acad. Sci.*, **68**, 1479; 1971) so it is possible that a change in binding may also occur at the nuclear level. Kirkpatrick *et al.* found that nuclear binding was low in the responsive cells, but do not mention the unresponsive ones.

A study such as this has several aspects that are relevant to tumour biology. First, it indicates that receptors are involved in steroid mediated inhibitory as well as activation processes. Second, it suggests that receptors may be translatable into clinical tests for the hormone responsiveness of human tumours; it is of considerable practical importance to decide which breast cancer patients will benefit from ablative endocrine surgery and oestrogen-binding experiments look hopeful in this respect. Third, the presence of a regulatory protein in a responsive cell and its loss or diminished binding potential in unresponsive cells (none of the experiments distinguishes between these two possibilities) have obvious analogies with enzyme induction in microorganisms.

AIRCRAFT DYNAMICS

Scheme of Notation

from a Correspondent

THE basic equations of aircraft dynamics are those of classical mechanics, with the elaboration that the forces and moments of aerodynamic origin are themselves influenced by the motions which occur. Aeronautical engineers are greatly addicted to dimensionless expressions because, when used with discernment, they often render generalities more apparent, increase the clarity of the work and yield succinct results. The equations of motion of an aircraft, together with appropriate systems of symbols, have therefore been the subject of much dimensionless invention for more than half a century.

The most familiar system in the United Kingdom has been that of Bryant and Gates (Aeronautical Research Council Reports and Memoranda (R&M) No. 1801; 1937) which separately defined dimensionless aerodynamic derivatives and inertial parameters. In the United States, a somewhat different system with broadly the same intentions was adopted. There have also been sundry variations on these themes and—to borrow a felicitous phrase from the latest number in the R&M series—the “clash of symbols” has been considerable. Moreover, the pre-war systems were devised largely in the context of small perturbations from a simple undisturbed condition, using only first-order derivatives. The behaviour of modern aeroplanes and the increasing importance of cross-coupling effects, the demands of aeronautical engineers concerned with missiles and the use of computers has rendered such systems inadequate.

R&M 3562 (H. R. Hopkin, *A Scheme of Notation and Nomenclature for Aircraft Dynamics and Associated Aerodynamics*, Parts 1 to 5, HMSO, 1970, £6.75) proposes a unified system of notation and nomenclature for the study of aircraft dynamics which seeks to avoid the limitations of the earlier systems, to be more self-consistent and to be capable of further expansion. It is the product of some years of discussion at the Royal Aircraft Establishment in cooperation with the National Physical Laboratory and is a most comprehensive and closely argued work. In the course of explaining the basis of the new system, it presents a useful survey of the whole of the fundamental concepts and definitions used in the field. The geometry associated with aircraft attitude, incidence and axis systems is presented in detail, although the quality of the diagrams is no more than adequate—rather better ones are provided in the Engineering Sciences Data Unit (ESDU) Data Sheets published by the Royal Aeronautical Society. The basis

of the system is, inevitably, somewhat similar to that of R&M 1801 save that it has been recognized that it is preferable, in defining “normalized” or non-dimensional quantities, to treat the aerodynamic data and the equations of motion in slightly different ways. The dynamic-normalized system is intended for investigations of the dynamic behaviour of an aircraft of certain mass acted on by aerodynamic and other forces when travelling at a certain speed. The aero-normalized system is convenient for expressing functions of the aerodynamic forces acting on an object of certain dimensions when it is in a stream of air moving at a certain speed. An important change, compared with the previous British system, is that the unit of force is now the datum dynamic head multiplied by an area, as opposed to twice this quantity. The characteristic lengths are now the mean aerodynamic chord for longitudinal quantities and the span for lateral quantities. The new aero-normalized derivatives are therefore similar to the “old” derivatives (and are denoted by similar symbols) but differ, in some cases, by factors which may involve powers of two and ratios such as the mean aerodynamic chord of the

tail moment arm. “Concise” derivatives are introduced, obtained by dividing a derivative by the appropriate inertial quantity and incorporating a sign change so that most derivatives become positive (for example, $m_q = -M_q / I_y$). The system is then arranged so that the equations of motion have the same form whether they are dimensional or non-dimensional. The precise significance of a symbol can, if necessary, be made explicit by a suitable “dressing”, but in most cases the context will be such that the dressings can be omitted, as has mostly been done in the ESDU Data Sheets. As Hopkin observes, however, “the undressing of symbols should be discreet”. In the absence of dressings, the symbols will look very similar to those of the older system although their numerical values, signs and non-dimensionalizing factors will usually be different. Until the new system has gained general acceptance, authors should be careful to explain exactly how they are using it.

The Engineering Sciences Data Unit has already issued several Data Sheets on Aeronautical Dynamics using this system, and it seems that it will have the blessing of the International Organization for Standardization.

Understanding the Origin of Petroleum

FATTY acids have long been regarded as possible predecessors of n-paraffins in petroleum. Some years ago Jurg and Eisma (*Science*, **144**, 1451; 1966) heated behenic acid ($C_{21}H_{43}COOH$) with kaolinite and with kaolinite and water for varying lengths of time and produced small amounts of n-paraffins—principally $C_{21}H_{44}$ —and unsaturated hydrocarbons and fatty acids. In next Monday's *Nature Physical Science* Shimoyama and Johns describe an experiment in which they heated the same fatty acid in the presence of Ca-montmorillonite.

The chief product was insoluble material deposited on the clay which they describe as kerogen-like. As in Jurg and Eisma's experiments the chief n-paraffin product was $C_{21}H_{44}$, formed by decarboxylation of the fatty acid. Smaller quantities of n-paraffins down to C_{16} were determined, and generally smaller amounts of n-paraffins in the C_{22} to C_{28} range. No fatty acids were detected in the products in contrast to Jurg and Eisma's findings and also to expectations based on their proposed reaction scheme. Failure to find new fatty acids may result from the use of Ca-montmorillonite instead of kaolinite or such acids, although formed, may have lost their identities by firm attachment to the kerogen-like product.

The production of $C_{21}H_{44}$ seems to have been halted by poisoning of the clay catalyst by the kerogen-like material.

Shimoyama and Johns conclude that the C_{16} and C_{17} n-paraffins are produced by breakdown of the C_{21} paraffin, whereas C_{18} , C_{19} and C_{20} develop in the early stages directly from the fatty acid and later by disruption of $C_{21}H_{44}$. Composite plots of amounts of individual n-paraffins and behenic acid against time show the braided form suggested by Hobson (*Earth Sci. Rev.*, **2**, 257; 1966) for a breakdown sequence $A \rightarrow B \rightarrow C \dots$. The dual origin of C_{18} , C_{19} and C_{20} yields hybrid curves.

With increasing age and maturity the larger n-paraffins in sedimentary rocks show a decrease in their carbon-preference indices, a measure of odd-carbon number dominance in the distribution of the molecules. Shimoyama and Johns's data for the C_{16} to C_{20} range show a comparable decrease with increase in time of heating and increase in temperature. But limited data on the C_{22} to C_{28} range show even-carbon number dominance, an unusual condition. Kvenvolden and Weiser (*Geochim. Cosmochim. Acta*, **31**, 1281; 1967) have noted a crude oil in which there is even-carbon number dominance in the C_{20} to C_{26} range and odd-carbon number dominance in the C_{27} to C_{33} range.

Tentative calculations based on the experimental data suggest the attainment of “mature” n-paraffin distributions under conditions approaching geological requirements of time and temperature.

SEAFLOOR SOILS

Engineering Properties

from a Correspondent

MOST of the surface of the Earth is covered by a film of marine soil, the properties of which determine the cost, hence the feasibility, of constructing on the seafloor all things from observatories to drilling installations. Do marine soils which have been recently deposited have a finite strength? A symposium to consider how best to cope with the fragility and other peculiarities of soils which have never dried was held from July 26 to 29 at the University of Washington, under the auspices of UNESCO and the National Science Foundation.

Charges on the sides and ends of settling particles cause marine soils to have an open, card-house fabric which is subject to collapse. Their sensitivity to stress is consequently extreme and disturbance may cause their strength to drop to a substantial degree. Dr D. G. True (US Navy Civil Engineering Laboratory, Port Hueneme, California) considered how best to measure the sensitivity of soils *in situ*, because it is impossible to transfer samples to the laboratory without changing them. A shear tester forces into the soil a cone or vane to about 3 m, then rotates it at one revolution per hour to measure "undisturbed" strength; this is re-observed after remoulding the sample by rotation at ten revolutions per minute.

An outline of current information about seafloor spreading by Dr R. S. Dietz (National Oceanic and Atmospheric Administration, Miami, Florida) made plain how profoundly tectonic processes affect everyday affairs; the areas adjacent to the continents are those which would be most useful for buildings, yet these are the areas of greatest instability. In some areas, for example the foreset slopes of major deltas and the flank of oceanic trenches, it may always be impossible to install permanent structures, because any disturbance could induce the downhill slide of sediments which have accumulated for millennia.

A theme present throughout the meeting was reminiscent of the exploration of space; is reward maximized by investing resources in a small amount of manned exploration, or in a comparatively large amount of purely instrumental exploration? Although submarine vessels have penetrated the deepest areas of the oceans, it is apparent that locomotion and manipulation in great depths remain awkward and expensive. Dr I. E. Mikhaltsev (Institute of Oceanology, USSR Academy of Sciences) made plain the advantage of operating on the seafloor rather than at the phase and storm

interface occupied by surface vessels. This and other contributions brought into relief the fundamental importance of television as a means of controlling both manned and unmanned devices.

The strength of marine soils is difficult to assess because there is only a limited time in which to apply tests. Geophysical techniques, usually acoustic, encounter this difficulty in extreme form, because the stress used in tests lasts for only a fraction of a second. Dr D. Taylor Smith (University of North Wales) showed that such factors as acoustic attenuation bear a useful relationship to geotechnical properties including porosity, itself descriptive of long-term strength. Drs R. C. Bostrom and M. A. Sherif (University of Washington) pointed out that in sediment piles slopes diminish until stability is reached, so that seafloor topography is a description of long-term strength and can be used to quantify it. The stress is that of infinite period applied by gravity. The most urgent need, perhaps, is the development of a technique capable of observing long-term strength from a ship under way.

A special topics session discussed, among other things, the use of marine soils to cover waste material. It transpires (Dr B. Lehman, Lockheed Building and Construction Corporation) that it would cost \$5 per ton to transport compressed waste from New York to the nearest tectonic trench, as against \$10 to \$20 to incinerate it. In an area penetrated by channels the bottom soil acts as a natural seismic recorder (Dr R. E. Sylwester and others, University of Washington) so that it is possible to map active fault traces invisible on land.

MICROEARTHQUAKES

Geothermal Fault

from our Geomagnetism Correspondent

THE discovery that fluid injection may produce seismic activity along previously inactive faults could prove to be the most socially significant geophysical advance of the century should it prove possible to apply it to the gradual release of strain in active, and potentially dangerous, faults. At present, however, the successful modification and control of earthquakes are far from reality, and a greater understanding of the fundamental processes involved will be required before such hopes can progress much beyond the theoretical stage. Work proceeds in the meantime on several fronts which range from controlled experiments away from human habitation to the observation of natural events and seismic situations created inadvertently by man himself.

Perhaps the most obvious situation in

which nature provides its own fluids is the geothermal field; and it seems likely that such fluids will have some effect on faults which cross the field. It is possible, of course, that faults in geothermal regions might be active even in the absence of fluids; but what is quite certain is that microearthquakes are observed in many major geothermal areas such as those in Japan, California and Iceland. And as Ward and Jacob (*Science*, **173**, 328; 1971) now show from a study of the Achuachapan Geothermal Field at El Salvador (Central America), these microearthquakes may be used to map active faults. Indeed, where large earthquakes are either rare or completely absent microearthquakes may provide the only means of fault mapping.

As it happens, between 1961 and 1970 the US Coast and Geodetic Survey reported thirty-two events with magnitudes greater than 3.5 and having epicentres within 60 km of Achuachapan; but depths of focus ranged from 16 to 276 km, so that it seems unlikely that these events were related directly to near-surface geothermal activity. By contrast, between December 7, 1969, and August 10, 1970, Ward and Jacob detected about 500 microearthquakes with magnitudes ranging down to 0. From the distribution of S-wave minus P-wave arrival times it is clear that two groups of events were present. Some 350 of the events had S-P times of more than 8 and were probably associated with a seismic zone which dips north-eastwards under El Salvador. But almost all of the remaining 150 or so had S-P times within the range 0-2; and it is these which were apparently related to surficial geothermal activity. These local events frequently occurred in swarms of ten to twenty events separated in time by up to several weeks. Unfortunately, because of operational problems the foci of only seventeen of the local microearthquakes could be located with any degree of precision, but these were sufficient to define a fault plane intersecting most of the foci and passing through a point where fault breccia was observed in a drill hole. This plane was roughly parallel to normal faults previously mapped to the north-west.

This is not the first time that microearthquakes have been used to map an active fault; but it is a significant case because of the association with geothermal fluids. Thus Ward and Jacob interpret the detected fault as the one which allows the hot geothermal water to reach the surface. If this is a valid interpretation the technique should prove to be of economic importance in that it would be of obvious advantage to site geothermal production wells close to the chief source of upwelling hot water.

Statistical Mechanics and Quantum Mechanics

G. E. UHLENBECK

Rockefeller University, New York

Part of the acceptance speech on the occasion of the award of the Lorentz Medal by the Royal Netherlands Academy of Sciences on June 27, 1970.

ARE the problems of statistical mechanics truly fundamental? I have often changed my opinion and now I would like to elaborate on it. When I was a young student, kinetic theory of matter seemed to me an example of a theory which truly explains something. With much care and effort I worked my way through the *Lectures on Gas Theory* by Boltzmann and the *Elementary Principles of Statistical Mechanics* by Gibbs. Much escaped me and became clear only after I read the famous encyclopaedia article by the Ehrenfests. It was a revelation, not only because of its great clarity but also because it contained a careful summing up of the series of more than twelve *lacunae* in the work of the masters. These were like frontier posts and a young student could thereby learn where the real problems lay. How difficult it is to find this out nowadays. The present pollution of the scientific literature makes the finding of clear water, the fundamental concepts, an extremely time consuming occupation. This is true not only for the new student but for anyone who tries to learn something outside his own speciality, as I well know by experience.

Though I passed my examinations successfully, I knew very little of quantum theory and even less of the theory of spectra. I learned that, with Goudsmit's help, when I returned from Rome in 1925 and became Ehrenfest's assistant. I shall not elaborate on the collaboration with Goudsmit, which I shall never forget and which led to the discovery of electron spin. Both Goudsmit and I have often related our memories of this unforgettable period and I mention it only because at that time my conception of statistical mechanics changed completely. I considered it to be clearly on a secondary level. Quantum mechanics on the other hand provided a foundation from which everything should follow, including the behaviour of gases, liquids and solids. This seemed to be confirmed by the success of the electron theory of metals. Pauli and Sommerfeld (both recipients of the Lorentz Medal) showed how all difficulties disappeared as soon as one applied the true quantum statistics. A few riddles remained, such as superconductivity, but in our optimism we felt sure that all would be straightened out eventually. My dissertation in 1927 about statistical methods in quantum theory was therefore a kind of optimistic synthesis of the encyclopaedia article of the Ehrenfests and the new quantum mechanical ideas. The number of unproved assumptions was reduced to three.

Later in Ann Arbor, the beautiful experiments of N. H. Williams on thermal noise and shot noise aroused my interest in the theory of Brownian motion, one of the nicest applications of statistical mechanics. I thought it very interesting but of course it was not fundamental. I remember very well

that when I told Pauli about it he called it "desperation physics". I didn't like this but I really agreed with him. For a physicist of the quantum mechanics generation to which I also belonged, the fundamental problems of the 1930s were the theory of the positron, quantum electrodynamics and the developing theories of nuclear structure and beta radioactivity; these were the things on which to work.

Let me say at this juncture that the image of progress in science as a kind of conquest of an unknown domain with a definite "frontier" and successive "breakthroughs" seems to me more and more to be only a romantic illusion. This picture was clearly inspired by the great breakthrough of quantum mechanics and it has influenced my judgment for a long time. I might even say that I was afflicted by it.

My opinion about the fundamental character of statistical mechanics began to change in 1937 to 1938 when I, together with Boris Kahn, became involved in the so called condensation theory. The question why a gas condenses below a sharply determined critical temperature at a sharply determined density has never been called to attention since Van der Waals and the proper understanding of it seemed difficult to us. During the lively discussion about this question at the Van der Waals Congress in 1938 it was even doubted whether the basic assumptions of statistical mechanics contained the answer even in principle. This doubt was not justified, but it made a deep impression on me. As long as such common phenomena as the equilibrium between liquid and vapour and the existence of a critical temperature were not truly understood, the field was not yet conquered, not everything had been explained in principle and thus there existed fundamental aspects of statistical mechanics which I had not appreciated.

(When I showed Pauli the article by Kahn and myself on condensation theory he looked at it and said, "Yes, one should read this". He did so and ridiculed somewhat the quasi-mathematical rigour of our work but I believe that he appreciated the fundamental character of the problem.)

After the war, I continued to follow the new developments in quantum electrodynamics and the theory of beta radioactivity, and from time to time I contributed a little. But my interest moved more and more towards the fundamental questions of statistical mechanics. In the 1950s I began to write a book on statistical mechanics with my pupil and friend, the late T. H. Berlin. I hoped that it would become a modernized and expanded version of the encyclopaedia article which had made such an impression on me. I hoped that we could determine the foundations of the theory in the same critical way as the Ehrenfests, and that we could make clear the nature of the still unsolved basic problems. In short, I hoped that we could discover the "structure" of statistical mechanics.

We worked hard on it but did not get very far and the sudden death of Ted Berlin in 1962 makes it doubtful that our plan will ever be realized. I have learned a lot from it, however, and I have the feeling that I more or less understand the structure of classical statistical mechanics at least. I believe that one always has to keep in mind that the task of statistical mechanics is to study the relationship between the macroscopic description of

physical phenomena and the microscopic molecular description. These two pictures are in a certain sense independent; moreover, they are, so to speak, on a different level and are therefore, even qualitatively, totally different. If one sticks to this idea, one can see that Boltzmann, Gibbs, Einstein, Ehrenfest and Smoluchowski have formulated the true basis on which one has to build further. One sees also that there are still many unsolved problems, such as condensation and other so called phase transitions, on which much work is being done. All these problems are very difficult but they are, as a mathematician would say, *bien posés* and therefore one can work on them.

In my opinion the situation is somewhat different for quantum theory. The relationship between the classical and quantum mechanical descriptions of molecular phenomena is rather clear, but this is not so for quantum mechanics and the macroscopic theory. I am aware that this opinion is not shared by most of my colleagues. I believe that the most widespread opinion is that quantum mechanics can be "grafted" onto the classical statistical mechanics of Boltzmann and Gibbs and that therefore quantum mechanics does not require anything essentially new. I had thought so earlier too, but I have slowly retreated from that conviction. The recent discoveries of so called macroscopic quantization and interference phenomena in liquid helium and superconductors have had a great influence on my ideas. They seem to me to show that the existing theories of superconductivity and superfluidity do not provide a complete explanation and that the true macroscopic description of the superfluids has not yet been found. It would be no surprise to me that this is so because the foundations of quantum statistical mechanics have not yet been sufficiently clarified. One only needs to think of the persistent currents to feel doubt about the

general validity of the ergodic theorems in quantum theory. Questions like these make low temperature physics so fascinating for me; they have had a rejuvenating effect on me and I am convinced that there is still much to be done on this "frontier" of physics and that profound surprises are possible.

Because I use the word "frontier" let me finally return to the romantic image of advances in science which I sketched earlier. I do not believe in it any longer. There are many frontiers and it comes down to the fact that in science one can only sometimes talk of progress. Whenever there is an advance there is a frontier, not the other way around. As to the direction of the advance, every investigator follows his own nose and does what he can. In my opinion this applies equally to space travel and to high energy physics and radio astronomy. These pursuits exist because they are possible and as long as the expense does not become too exorbitant one must, of course, continue them. But I think that one must oppose all fashion and prestige arguments. There is no natural hierarchy of problems and moreover, as Poincaré remarked long ago, a problem is never completely but always only more or less solved.

It seems better to me to view progress in science as the expansion of different circles of investigation, each autonomous and often apparently entirely independent of the others. The deep problems are to determine how these areas hang together, and how one can arrive at a larger unity. Biology and physical-chemical research, for example, form two such large circles. Their interrelationship seems to me to represent one of the deepest questions man can ask, a real *mysterium tremendum*. On a much smaller scale macroscopic and molecular physics form two such circles and statistical mechanics attempts to fathom their relationship.

Research Environments and Productivity

S. P. GUPTA & K. D. SHARMA

Research Survey and Planning Organization, CSIR, New Delhi-1

The productivity of Indian scientists has been investigated with a view to identifying the environmental factors that influence it. These findings may help policy makers and science managers to create the necessary environmental conditions.

OUR study of productivity has been based on data collected for a report called *Opinion Survey of Scientists and Technologists*¹. About 9,000 questionnaires were sent to the heads of all the national laboratories, other government and autonomous research institutions, private/industrial research organizations and departments of science, engineering and medicine in universities. The heads of institutions were

requested to distribute the questionnaire among an approximately equal number of researchers not below the rank of

Table 1 Characteristics of the Sample

Characteristics: age group	Per- centage	Characteristics: organizational settings	Per- centage
21-25+	1.9	National laboratories	18.1
26-30+	17.9	Govt. res. institutes	22.2
31-35+	26.7	Private/industrial res. institutes	6.2
36-40+	26.3	Univs./teaching institutes	53.5
41-45+	12.1		
46-50+	8.2		100.0
51-55+	4.5	Years since PhD	
56-60+	1.0	0-5+	45.6
Above 60	1.4	6-10+	30.6
		11-15+	13.5
		16-20+	5.8
Total	100.0	Above 20	4.5
Median age (36.6)			
		Total	100.0

Table 2 Average Publication per Year with Standard Deviation for PhD Scientists according to Age Groups

Age groups	No. of respondents	Mean * publications per year	Standard deviations
21-25+	10	1.3	1.6
26-30+	92	1.8	2.5
31-35+	137	2.4	3.5
36-40+	135	2.6	3.4
41-45+	62	3.2	4.5
46-50+	42	2.7	3.0
51-55+	23	4.6	3.9
56-60+	5	3.4	2.1
Above 60	7	2.8	2.2
Total	513	2.6	3.4

* Statistically significant at 0.05 level.

laboratory assistants. No information was available as to how the distribution in each institution was effected, but the sample seems fairly representative of various ranks and disciplines.

An important factor influencing the size and composition of the sample was the willingness or unwillingness of heads of institutions to cooperate. In the absence of a roster of Indian scientists and of the ability to collect the data personally, the only course was to approach the respondent through heads of institutions to ensure a maximum, rapid return. But in many cases cooperation could not be obtained and, as a result, some institutions returned no questionnaires. In all, about 2,300 replies were received in five months—roughly a 25% return. After several rejections due to incomplete information, the total sample analysed stands at 2,143.

We have considered PhD scientists only because scientific productivity is assessed in relation to "professional age"² (the number of years since obtaining the PhD). Table 1 summarizes the important characteristics of the sample considered in this article.

We have measured scientific productivity by objective criteria, such as the number of papers, books and patents published. In constructing the index of productivity, a book was considered equivalent to four scientific papers in terms of contribution and efforts².

Individual Variables and Productivity

In the first stage of analysing our findings, we tried to discuss some major individual variables, such as age and place of work, with relation to productivity. Table 2 shows the mean number of publications per year and standard deviations in different age groups and also for the combined groups. The age of the respondent varied from 21 to 65, with a median age of 36.6 years, and the mean output of the combined groups during the period under study was 2.6 publications per year. The consistent upward trend in publications with age is indicated up to the age of 55, after which it decreases. The average number of publications per year is highest in the

Table 3 Average Number of Publications per Year with Standard Deviation according to Four Organizational Settings

Organizational setting	No. of respondents	Mean * publications	Standard deviation
National laboratories	93	2.2	2.4
Government research institutes	114	2.9	3.6
Private/industrial research institutes	32	2.6	4.3
University/teaching institutes	275	2.6	3.4
Total	514	2.6	3.3

* Not statistically significant.

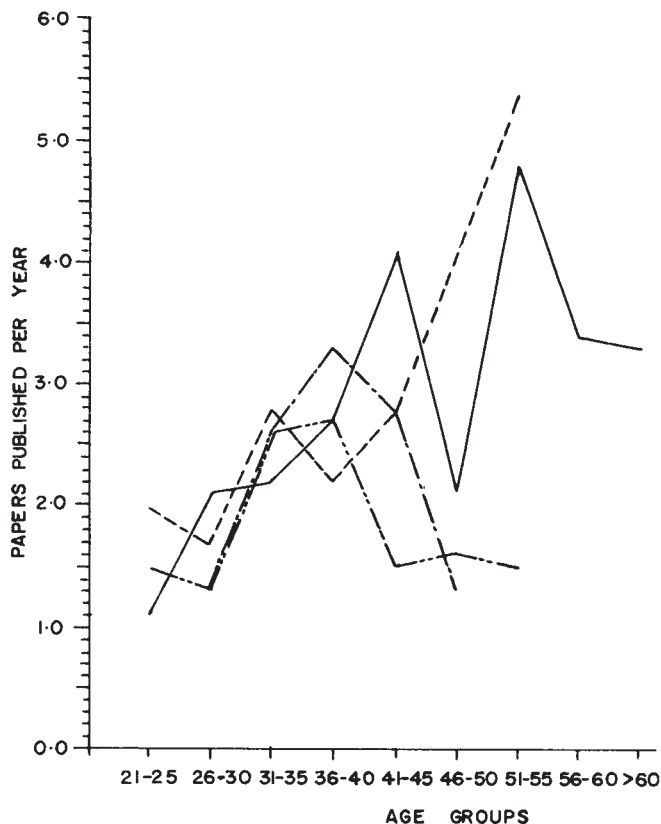


Fig. 1 Productivity of scientists in different age groups and types of organization. —, National laboratories; ---, government research institutions; - · - · -, private industrial research institutions; — — — —, universities and teaching institutions.

age group 51-55. When group means within each category are compared, the findings are statistically significant at the 0.05 level.

Agewise Productivity

Table 3 shows that organizational setting has no influence on the mean publication rate. The insignificant difference between the mean number of publications in different organizations could be due to large variance within each category. Hagstrom³ finds considerable differences between the contributions of industrial and academic scientists to the growth of science. This is because the managers of industry are anxious to see the findings of their research scientists fully covered by patents before publication in scientific journals. The results of our study do not support Hagstrom's hypothesis. In India, it is quite likely that industrial management puts no constraint on the publication of papers in scientific journals.

Fig. 1 shows the productivity of scientists for different age groups in various organizations. In national laboratories the productivity rate seems to be highest when scientists are in their late 30s and the curve shows a sharp decline thereafter. A similar trend is evident for the scientists in private and industrial research institutes. The findings for these two types of organization are consistent with those of Lehmann⁴ and Meltzer⁵, who found the greatest productivity in the late 30s and early 40s, followed by a decline.

There is a trend for scientists in government research institutions to increase in productivity between 40 and 55. In the university and other teaching institutes, the productivity increases constantly until the early 40s and then declines between 45 and 50. After that the curve shows an upward trend in the early 50s, before relapsing again. In spite of overall differences in slopes, there are some remarkable similarities among these curves. The ages of best achievement

Table 4 Average Number of Papers in Relation to Recognition in Various Age Groups

Age group	Recognition	
	High	Low
21-25+	2.0	1.5
26-30+	2.4	1.9
31-35+	2.9	2.2
36-40+	2.8	2.2
41-45+	2.3	2.7
46-50+	3.5	2.3
51-55+	3.1	5.0
56-60+	NA	NA
Above 60	NA	NA

in national laboratories, private and industrial research institutions, and to some extent universities and other teaching institutions, are quite similar. The late 30s and early 40s are the most productive periods in the lives of scientists except for those working in government research institutions.

Recognition, Age and Productivity

Recognition is an indicator of scientists' merit and social worth. In science, two most general forms⁶ of recognition are: the immediate supervisor's evaluation of current research work and the credits for research publications. For our study recognition was measured largely through self-evaluation by the respondents themselves. If the respondent felt that he was highly appreciated by his supervisor and given preference in authorship, it was taken to indicate high recognition, otherwise he was categorized as having low recognition.

When recognition is examined in relation to productivity, keeping age groups constant, the results are quite interesting (Table 4). Productivity is low for scientists with low recognition. Although recognition is important to all scientists, younger scientists are more concerned about it, for they feel that it is essential if they are to establish themselves. Therefore, one of the environmental condition conducive to higher productivity in younger scientists is recognition. Another important outcome of Table 4 is that after the age of 50 organizational recognition is not important in the productivity of scientists, perhaps because at this age they are well established.

Freedom and Productivity

We have inferred the extent of freedom in research from the extent of autonomy in the selection of projects. Like the index for recognition, this has been reduced to two classes—high and low degrees of freedom.

Table 5 Publication per Year as Related to Freedom in Various Organizations

Organizational setting	Freedom		P*
	High	Low	
National laboratories	2.4	2.0	n.s.
Government research institutes	3.4	2.2	0.05
Private/industrial research institutes	3.2	1.6	n.s.
University/teaching institutes	2.8	2.1	n.s.

* Significant level.

Our chief concern was to find out how scientists perform in these two categories of freedom. Table 5 shows the publications per year in various organizations where freedom is variable. It shows that the average number of publications per year is greater when there is a high degree of freedom than when there is a low degree of freedom in all four organizational settings. The differences within the organization were not statistically significant, however, except in government research institutes (other than national laboratories). It seems paradoxical that professional freedom has

no bearing on productivity. In our study the emphasis was on freedom to select research projects, whereas a scientist is probably more concerned with the freedom to attack the problem and comparatively less bothered who selects the project for him. It is quite likely that the scientist wants least interference in his day to day work.

Prospects for Future Productivity

The results of our study present an interesting picture of Indian science. For the total sample productivity increases until the age of 55, and then declines. This contrasts with the finding of Pelz and others⁷, and so this aspect was studied in detail for each organization (Fig. 1). It can be seen that productivity increases with age for: (i) government research laboratories, and (ii) teaching institutes and universities. In the case of national laboratories and private industrial research institutes the trend follows the international pattern, but for government laboratories and universities it shows a secular increasing trend, for which there is no obvious reason. Perhaps in government research laboratories and universities and teaching institutes authorship is based on seniority in the administrative hierarchy. But there may be other reasons, and it would be interesting to identify the factor responsible for the continuing increase of productivity with age in these institutes. It might then be possible to replicate these conditions in other institutes to augment the productivity of Indian scientists.

Scientists in national laboratories are less productive than their counterparts in organizations such as government research institutes; private and industrial research institutes, universities and so on. It is also evident that scientists in government research institutes have the highest productivity. It is interesting that this correlates with increasing productivity with age. This again tends to support the hypothesis that in government organizations, it is the hierarchy that decides the authorship rather than the actual participation in the research project.

Recognition and freedom have been suggested as motivating environmental factors which influence the productivity of scientists. From the operative point of view, the influence of these factors varies with age. We have found that people in the higher age group are neutral to recognition while those in the younger age group seem to be very susceptible to it. The lack of influence of freedom to choose projects on productivity needs to be studied further in view of the fact that the conflict between administrators and scientists revolves round control and freedom. In another study (unpublished) we found that freedom was a neutral factor with regard to the commitment of scientists to organizational goals. This could be explained by a lack of precision in the definition of the term "freedom" in the questionnaire, or a difference of opinion among scientists about the meaning of the term. In India scientists seem to be indifferent to this type of freedom. They probably interpret freedom as the opportunity to attack a problem without hindrance.

We have attempted to isolate a few of the environmental variables which influence the productivity of scientists. If these factors are properly manipulated, it is possible to increase productivity, and so it is essential that policy makers should consider these aspects more seriously.

¹ Ahmed, A., and Gupta, S. P., *Opinion Survey of Scientists and Technologists*, Survey Rep. No. 9 (RSPO, CSIR, New Delhi, 1967).

² Crane, D., *Amer. Sociolog. Rev.*, **30**, 699 (1965).

³ Hagstrom, W. O., *The Scientific Community*, 38 (Basic Books, 1965).

⁴ Lehmann, H. C., *Age and Management* (Princeton University Press, 1954).

⁵ Meltzer, L., and Salter, J., *Amer. Sociolog. Rev.*, **27**, 351 (1962).

⁶ Glaser, B. G., *Social Problems*, **19**, 268 (1963).

⁷ Pelz, D. C., *Trans. IEEE on Engineering Management*, EM11, 23 (1964).

Unique Bedrock and Soils associated with the Teesdale Flora

G. A. L. JOHNSON & D. ROBINSON

Department of Geology, University Science Laboratories, Durham

M. HORNING

Nature Conservancy Research Station, Bangor

This article describes the geological factors which have contributed to the formation of the unique bedrock geology and soils of the metamorphosed limestones on Widdybank and Cronkley fells in Upper Teesdale. The survival of the relict arctic-alpine flora is probably directly related to the distinctive geology of the area.

THE distinctive relict arctic-alpine flora of Upper Teesdale, Co. Durham and North Yorkshire, has been famous in biological circles for more than a century. In a subarctic environment, not quite warm enough for the growth of trees, there occur many species of flowering plants, pteridophytes, bryophytes and lichens which are rare in the British Isles and a few species which are not known in Britain outside Teesdale¹⁻⁴. The flora includes a number of plants belonging to widely differing phytogeographical groups and has been interpreted as a relict flora from the vegetation that colonized Teesdale shortly after the end of the Quaternary glacial period. The flora has survived through the post-glacial forest and blanket bog intervals in Teesdale partly on rendzina soils associated with rotted crystalline marble on Widdybank and Cronkley fells^{1,3}.

Stratigraphy and Structure

The structure of Upper Teesdale is dominated by a north-south trending, east facing faulted monocline called the Burtreeford Disturbance⁵ that has an eastward downthrow of some 200 m (Fig. 1). On the west, upfaulted side of this structure, Skiddaw Slates and tufts of Ordovician age are exposed in the sides of the Tees at Pencil Mill, forming a small and poorly exposed inlier in the valley floor⁵. An angular unconformity separates the folded Ordovician from the overlying almost horizontal Carboniferous marine strata. The Carboniferous sequence⁵ commences with a Basement Group composed of conglomerate and sandstone beneath dark limestones and shales about 25 m thick. The succeeding Lower Limestone Group is dominated by the Melmerby Scar

Limestone, a light coloured limestone 38 m thick, which is separated into thick beds with thin shale and sandstone partings. Above the Melmerby Scar the upper beds of the Lower Limestone Group and the overlying Middle Limestone Group are composed of a rhythmic sequence of predominantly dark coloured limestone bands with intervening shales and sandstones. Significantly the Teesdale relict flora is found particularly in association with outcrops of metamorphosed light coloured Melmerby Scar and Robinson limestones and not with the overlying unaltered darker pigmented limestones.

It is probable that a full sequence of Carboniferous sediments was laid down in Teesdale followed possibly by Permian and Mesozoic deposits, but no evidence of these beds remains because of extensive Tertiary erosion which has removed any younger rocks.

Towards the end of the Carboniferous period uplift, compression and doming of the region took place and the Great Whin Sill quartz-dolerite intrusion was emplaced. The heat of intrusion baked and altered the sediments above and below the sill, producing new minerals and textures in the altered rocks contributing significantly to their present nature.

In Teesdale the Burtreeford Disturbance was active before the emplacement of the Great Whin Sill. The sill cuts across the faulted monocline from a position near the Tyne Bottom Limestone, within the Middle Limestone Group, on the east to a horizon near to the base of the Melmerby Scar Limestone on the west (Fig. 1). On the west of the disturbance the sill, 73 m thick, nears its maximum thickness and is at its lowest stratigraphical horizon. In all directions it tends to rise in the Carboniferous succession and decrease in thickness away from this centre^{6,7}.

After the emplacement of the Whin Sill, hydrothermal mineralization commenced in the Pennine region. This process is believed to have extended over at least 100 m.y. (ref. 8) producing economic galenabarytes veins in Upper Teesdale. The veins have been extensively worked in the region, notably at Cow Green Mine, and trial workings, chiefly for lead ore, are present on Widdybank and Cronkley fells.

A further important factor in the history of Upper Teesdale is the long period of erosion, perhaps 50 m.y. from the early Tertiary to the present day, that has removed the younger rocks and exposed the Whin Sill within the Melmerby Scar Limestone on the floor of the valley. The almost flat top of the sill forms a wide bench on Widdybank and Cronkley fells

and the overlying crystalline marbles outcrop extensively though often masked by superficial glacial drift. The morainic drift and peat deposits, formed during Quaternary glacial and post-glacial times, have also played a significant part in the formation of the biologically important soils.

Whin Sill and Metamorphism

On Widdybank and Cronkley fells metamorphism of the Melmerby Scar Limestone and associated sediments occurs above and below the Great Whin Sill. The limestone is recrystallized for more than 25 m from the contact and the metamorphic effect can be detected to almost 40 m above and

below the sill on the basis of spotting in shales. Elsewhere in northern England, where the sill is thinner, the effect of metamorphism is restricted to beds close to the contact, at a distance of 18 m above. The dark pigmented limestones, found principally in the Middle Limestone Group, are not recrystallized because the carbonaceous organic matter causes the suppression of marmorization¹⁰. Thus where dark limestones are found near the Whin contacts very little or no crystalline marble is found.

The formation of marble in Upper Teesdale is clearly the result of three factors combining to form a bedrock formation unique in northern England. First, the Whin Sill is near maximum thickness and lowest stratigraphical horizon.

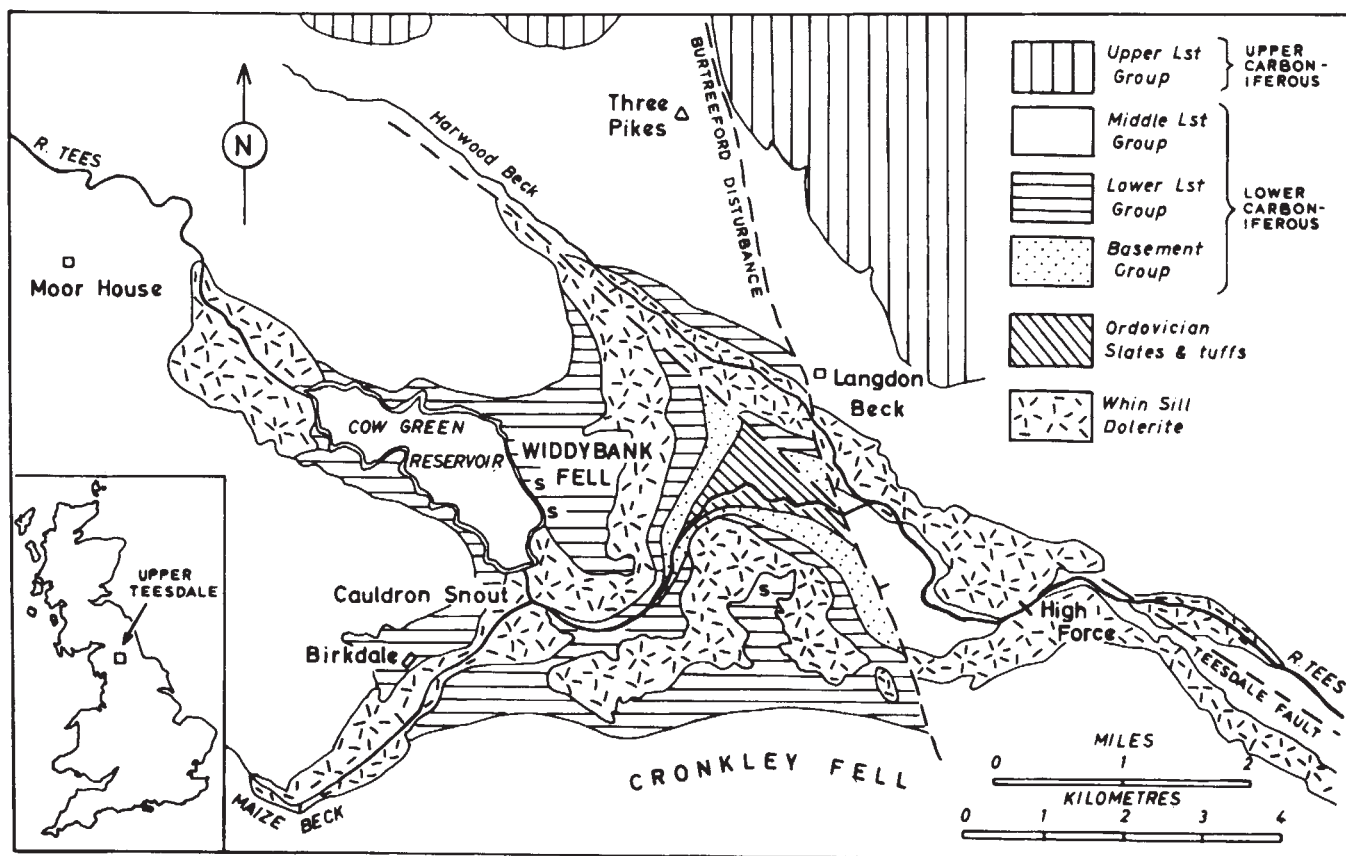


Fig. 1 Geological sketch map of part of Upper Teesdale showing the outcrop of the Great Whin Sill and the principal groups of sedimentary rocks. S, Well developed rotten marble and calcite sand rendzinas.

The alteration of pure limestones is limited to simple recrystallization. Impure limestones close to the contact form calc-silicate rocks in which a wide variety of minerals are present. Shales adjacent to the Whin Sill are converted into hard porcellaneous rocks (whetstones) in which the bedding is lost. Further from the contact spotted shales are commonly developed. Pure sandstones are converted into white quartzite at the contact and impure sandstones develop alteration patterns depending on the amounts of argillaceous or calcareous material present. The mineralogy of contact rocks associated with the Whin Sill in Teesdale has been described recently by Robinson⁹.

The pure Melmerby Scar Limestone of Widdybank and Cronkley fells is recrystallized by the Whin Sill to a saccharoidal marble for about 25 m from the upper contact; a small thickness of marble is also present below the sill. The marble consists of dodecahedral to rounded grains of calcite varying in average grain size from 0.5 mm at the contact to 0.05 mm

Second, the sill is injected into the thickest limestone in the Carboniferous succession of the region, the Melmerby Scar Limestone. Finally, the low carbon content of this pure, light coloured limestone allowed metamorphic recrystallization to take place readily, with the development of thick marble formations.

Weathering of Crystalline Marble

The marble outcrop is partly masked by patches and tongues of glacial drift on Widdybank and Cronkley fells. This is a pattern of exposure that has not changed greatly from the early post-glacial period when continuous vegetation cover stabilized the unconsolidated drift slopes. Since then peat has developed over impervious deposits, particularly the clay drifts, and thin soils have formed over exposed bedrock.

Weathering of bedrock crystalline marble takes place both at the surface, by processes of subaerial erosion, and below

the surface at the bedrock drift or mineral soil interface. At the surface a hardened crust tends to form on the marble and erosion may be relatively slow except near to the Whin contact where the coarsely crystalline rock is often readily attacked by subaerial weathering processes. At the subsurface junction of bedrock marble and overlying drift or soil, percolating ground water causes solution weathering leading to loss of cohesion between calcite grains in the marble. Sections through the drift-marble interface show rotten saccharoidal marble or calcite sand deposits 0.25 to 3.0 m thick. The thickness of the layer and the rate of weathering of the marble are dependent on the amount of ground-water movement. Subsurface erosion sufficient to produce hollows in the land surface has taken place as the rotted marble is removed in solution.

From these observations it follows that the unconsolidated calcite sand, known to a succession of biologists as "sugar limestone", is chiefly a subsurface weathering product of saccharoidal marble formed beneath a cover of drift and soil. Its presence at the surface today is caused by contemporary erosion of the soil and drift cover. Calcite sand is a most unstable surface deposit which tends to erode by rain and wind action at any place where the protective drift, soil or vegetation cover is removed. A cycle consisting of subsurface weathering below thin soil followed by erosion of unstable calcite sand may have taken place on crystalline marble outcrops on Widdybank and Cronkley fells during much of the post-glacial time. This would provide a succession of open habitats suitable for the survival of the arctic-alpine flora. Because of its instability and secondary origin it is unlikely that calcite sand deposits were present on these outcrops during the period of initial plant colonization in late-glacial times.

Soil Development

The presence or absence and thickness of drift cover have been important factors in determining the soils developed over crystalline marble on Widdybank and Cronkley fells. Under continuous drift, more than 60 cm thick, the limestone acts chiefly as a platform on which soil formation takes place in the upper layers of the drift cover. The limestone exerts some influence on soil formation by maintaining free drainage in the subsoil and lower drift, even though the latter is often of heavy texture. Peaty gleyed podzols or deep peat are the resultant soils. Where the superficial drift cover is thinner (30 to 60 cm) the limestone maintains free drainage, but also exerts an influence on the chemistry of the soil so that brown earths or brown calcareous soils result. Where there is only a thin layer of superficial material, less than 30 cm thick, the bedrock marble dominates soil formation and rendzinas are the resulting soils.

The rendzinas form part of a complex in which three subtypes, for the purpose of this paper called α , β and γ , occur in association with small areas of brown earth soils. The brown earths are found over patches of deeper superficial material. The rendzinas are characterized by alkaline reaction and excessive drainage such that even short dry periods cause a water deficit¹¹. Rendzina α is the simplest and forms *in situ* from rotten crystalline marble. The profile is divisible into a dark grey, humic but sandy surface horizon (A or A_h) which has a dense mat of fibrous roots, and an underlying C horizon of white or cream coloured calcite sand. Formation of α rendzinas requires the prior removal of any superficial drift with exposure of the underlying marble to subaerial erosion and soil forming processes.

Rendzina β is the most widespread in the rendzina complexes. It develops over crystalline marble bedrock in regions where drift parent materials play an important part in profile formation. A typical profile is composed of a thin horizon (up to 10 cm) of dark brown or reddish brown clay or silt loam over calcite sand resting on relatively unaltered marble. The colour and texture of the surface layer vary considerably.

Colour variation reflects a number of factors but bright coloured reddish variants have a high content of total iron present as hydroxides. The bright red soils overlie marble cut by fine siderite veins which oxidize to hydroxides of iron including goethite. The soils inherit their colouration and high iron content from the vein material, fragments of which are normally present in the soils. Textural variation depends on changes in the proportions of sand and clay with the silt fraction remaining fairly constant. The soils also contain small stones which have been derived from the surrounding drift. The loam is clearly of mixed origin containing contributions from the drift and the underlying marble; mixing probably took place during pedogenesis.

Rendzina subtype γ is a closely related group of soils which have aeolian erosion and depositional characteristics as a uniting feature. They form a small part of the total rendzina complexes and show much variation in detailed profile morphology. These rendzinas are particularly well developed in the Thistle Green area, Cronkley fell, where they are associated with and abut against bare areas of calcite sand. Profiles of rendzina γ almost always contain a number of buried surface horizons and clear evidence of surface accretion. Observation on a windy day immediately demonstrates that aeolian movement and deposition are active and sufficient to produce profile accretion. These soils were formed under conditions of periodic erosion, aeolian transport and deposition of calcite sand. Readily identifiable old surface horizons within the rendzina γ profiles support an origin by periodic deposition rather than continuous accretion. Periodic erosion of limestone sand would produce areas available for plant colonization and would aid the survival of the Teesdale flora.

The typical rendzina profiles differ markedly from soils developed over unaltered Carboniferous limestone though the rendzina β subtype grades imperceptively into normal limestone soils away from the Whin Sill contact as the bedrock changes from coarse to fine grained marble. The marble rendzinas, though distinctive, form only a relatively small part of the soils of the botanically significant region of Upper Teesdale. The brown earths, brown calcareous soils and the various gleys developed on drift and other parent materials are also important.

Bedrock-Soil-Flora Association

The combination of lower Carboniferous clear water limestone, late Carboniferous Earth movements and the injection of the Whin Sill produced coarse grained crystalline marble in Upper Teesdale. Tertiary and recent erosion with the Quaternary glaciation exposed this unusual bedrock at the surface. Rendzinas developed on outcropping marble by soil forming processes. A geological setting of this type is unknown outside Upper Teesdale in Britain and comparable rendzinas are similarly restricted. In the vicinity of this narrow geological and pedological setting the Teesdale flora has survived since shortly after the end of the Quaternary glaciation. It is our contention that the survival of the relict flora in association with unique geology and soils is not coincidental. The inherent instability and excessive drainage of the calcite sand soils have provided a continuous series of precarious habitats suitable for the survival of the alpine plants. In the vicinity of these soils elements of the flora have colonized restricted adjacent regions of differing soil type giving the plant distribution found today. Other factors have clearly played their part in sustaining the flora over the period of about 10,000 years. Two factors are particularly noteworthy; first, the severe climate of the Teesdale fells provides a suitable environment, and second, continuous grazing of the small areas of limestone grassland from prehistoric times¹² to the present day has tended to maintain the required more open habitats.

We thank Drs W. A. Clark, A. W. Davison, J. Turner and D. F. Ball who have read the manuscript and offered helpful advice. This research forms part of a survey of Upper

Teesdale supported by the Natural Environment Research Council.

Received July 12, 1971.

¹ Pigott, C. D., *J. Ecol.*, **44**, 545 (1956).

² Bellamy, D. J., Bridgewater, P., Marshall, C., and Tickle, W., *Nature*, **222**, 238 (1969).

³ Turner, J., in *Durham County and City with Teesside*, 123 (Brit. Assoc., Durham, 1970).

⁴ Bradshaw, M., in *Durham County and City with Teesside*, 141 (Brit. Assoc., Durham, 1970).

⁵ Johnson, G. A. L., *Trans. Nat. Hist. Soc. Northumb.*, **41**, 5 (1970).

⁶ Dunham, K. C., *The Geology of the Northern Pennine Orefield*, 1 (Mem. Geol. Surv. Gt. Brit., 1948).

⁷ Dunham, A. C., *Trans. Nat. Hist. Soc. Northumb.*, **41**, 92 (1970).

⁸ Dunham, K. C., Firch, F. J., Ineson, P. R., Miller, J. A., and Mitchell, J. G., *Proc. Roy. Soc., A*, **307**, 215 (1968).

⁹ Robinson, D., *Trans. Nat. Hist. Soc. Northumb.*, **41**, 119 (1970).

¹⁰ Robinson, D., *Cont. Min. Pet.* (in the press, 1971).

¹¹ Welch, D., and Rawes, M., *Trans. Nat. Hist. Soc. Northumb.*, n.s., **17**, 57 (1969).

¹² Johnson, G. A. L., and Dunham, K. C., *Geology of Moor House* (Nature Conservancy Monograph No. 2), 158 (1963).

Transitive Inferences and Memory in Young Children

P. E. BRYANT

Department of Experimental Psychology, University of Oxford

T. TRABASSO

Department of Psychology, Princeton University

Contrary to the conclusions of Piaget, young children can make transitive inferences if precautions are taken to prevent deficits of memory from being confused with inferential deficits.

FOR some time, it has been believed that young children are unable to form transitive inferences about quantity until they pass the stage of logical preoperations at about 7 yr old^{1,2}. This argument has been very widely accepted^{3,4}. Piaget and his colleagues propose that the young child cannot infer, for example, that $A > C$ from the information that $A > B$ and $B > C$. They assert that the child is unable to coordinate the first two, separate items of information in order to reach the correct inferential conclusion about A and C. If true, this claim has important educational implications, for a child who cannot combine this information must also be unable to understand the most elementary principles of measurement.

We report two experiments which show that the claim is unjustified. The experiments demonstrate that 4 yr old children can make transitive inferences about quantity, provided that they can remember the items of information which they are asked to combine.

One must ensure that the child has retained the comparisons which he has to combine, if one is to infer whether or not he can make transitive inferences. Otherwise, an error might simply be due to a failure in memory and have nothing to do with inferential ability. Yet experiments in which it is reported that children cannot make inferential judgments lack this elementary precaution. One can control for forgetting by taking two precautions. First, teach the child the initial comparisons ($A > B$ and $B > C$) very thoroughly. Second, test for memory of these comparisons at the same time as one asks

the inferential question about A and C. The first precaution ensures retention of the initial comparisons and the second checks for this retention during the inferential problem.

We found it necessary to introduce another control in our experiments. This was against the transfer of "absolute" responses. The general procedure in prior experiments has been to use three quantities (A, B and C). If only three are used, the correct response to the two extreme quantities must be the same in both the inferential problem and in the initial direct comparisons. The quantity A is the "larger" when compared with B, and C is the "smaller" when compared with B, in the initial direct comparisons. Yet "larger" is the correct response to A and "smaller" is the correct response to C in the inferential AC comparisons. Thus a child who produces the correct response when asked the AC question may do so by parroting a verbal label picked up during the initial comparisons, and not, as has always been assumed, by making a genuine inference through the combination of two separate comparisons.

The correct control is to introduce more stimuli and thus more direct comparisons. If there are as many as five stimuli (in descending order of size they are A, B, C, D and E) four initial direct comparisons are possible, $A > B$, $B > C$, $C > D$, and $D > E$. Note that B, C, and D all feature in two of these comparisons and that each of them is the larger in one comparison and the smaller in the other. This means that no one absolute response can be transferred to any one of these three quantities, and it therefore follows that the crucial transitive comparison will be between B and D. This indirect comparison cannot be solved by transfer of absolute responses, since B and D were both larger and smaller in the initial direct comparisons.

Our experiments thus involved first a thorough training period with four direct comparisons, followed by a test period in which the children were tested for their ability to make transitive judgments and to remember the initial comparisons. In the first experiment, sixty children in three age groups of twenty each participated. The mean ages of the groups were

4.5, 5.6, and 6.7 yr respectively. The youngest group came from a local nursery school and the older groups from two local infants' schools.

The training and testing materials were identical. Five coloured wooden rods, each of a different length and colour, were used. The lengths were coloured differently in order that they could be identified and remembered. Thus the child learned, for example, that blue was larger than red and red larger than green. The colours were red, white, yellow, blue and green, and the lengths were 3, 4, 5, 6 and 7 inches. The particular colour-length combinations differed from child to child and were counterbalanced within each age group.

The rods were presented in pairs throughout the experiment. The pairs were always presented in such a way that each rod protruded from the top of a container by one inch. The equal protrusion was achieved by sinking bores of different lengths in the container box. This kind of presentation forced the child to use the colour differences in making a choice between different lengths.

In the initial training, each trial consisted of showing the child a pair of rods of different colours, each rod protruding one inch from the top of the box. The child was asked to indicate which rod was the "taller" or the "shorter" ("big" and "little" were the terms used with the youngest group, as they were more easily understood). When the child made his choice the experimenter drew out the rods and held them perpendicular to the table, so that the child could compare lengths directly. This was the feedback for the choices in the direct comparisons, which enabled him to learn to make the correct choice. The question asked (taller and shorter) and the positions of the rods (left and right) were varied in an irregular order from trial to trial.

The training was divided into two phases. In the first, the four comparisons, $A > B$, $B > C$, $C > D$, and $D > E$, were trained separately and in order from either the tallest to the shortest or vice versa; half of the children in each group were trained with each order. Each of the pairs was learned to a criterion of eight out of ten successful choices. In the second phase which followed immediately, all four pairs were presented in a random order on different trials. This interweaving continued until each child responded correctly to six successive presentations of each pair.

Testing followed immediately after the completion of the second training phase. The testing procedure was the same except that no feedback at all was given, that is, the lengths were not shown after a choice. Each child was tested four times on every one of the ten possible pairs of colours. These ten included the four, initial (direct) comparisons, and six, new, transitive (indirect) comparisons. The order in which the pairs were tested was random and varied between children. The type of questions and the position of the rods in each pair varied irregularly as in training.

All groups learned the initial (direct) comparisons rapidly. In the first phase of the training there seemed to be no age differences in speed of learning. In the second phase, however, the 4 yr old children made more errors than the other two age groups who were not significantly different from each other.

The test results are summarized in Table 1, which gives the average probability of a correct response on each pair of colours for each age group. The main diagonal cell entries (A, B: B, C: C, D: D, E) of each subtable in Table 1 show the correct choice probabilities for the initial direct comparisons. The top row and the right column off-diagonal entries (A, C: A, D: A, E: B, E: and C, E) are those for transitive tests where one or both of the rods included one of the end points, which were always either larger (A) or smaller (B). (These transitive comparisons may have been susceptible to the transfer of absolute responses.) The critical entry is the off-diagonal B, D pair, in which each rod had been both larger and smaller in the initial comparisons. The importance of this cell is stressed.

The evidence for transitivity is impressive at all age levels.

All the transitive comparisons (AC, AD, AE, BD, DE, and CE) were well above chance level, since the upper 99% confidence bound on the hypothesis of chance is 0.65 with a sample of $n=20$. Turning back to the crucial BD comparison it should be noted that children at all three age levels were able to make genuine transitive inferences very well.

It should also be noted that the BD scores were consistently the lowest of all ten comparisons. Of particular interest is the fact that the children seemed to perform at a lower level with the BD comparisons than with BC or CD comparisons, and yet these last two provide the information on which the transitive BD judgment must be based. This conclusion is supported by an analysis of variance of the errors on these three comparisons, which produced a significant difference between pairs ($F_{3.3\%}$, d.f.2,114, $P<0.05$) and no interaction with age. Thus our conclusion from the first experiment was that young children can make genuine transitive inferences extremely effectively, but not perfectly. The reason for less than perfect inference is discussed later.

Table 1 Probability of Correct Choices on Tests for Transitivity and Retention (Experiment 1)

Stimulus	B	C	D		E
4 yr old children					
A	0.96	0.96	0.93		0.98
B	—	0.92	0.78†	(0.83)*	0.92
C	—	—	0.90		0.94
D	—	—	—		0.91
5 yr old children					
A	1.00	0.96	1.00		0.98
B	—	0.86	0.88†	(0.80)*	1.00
C	—	—	0.92		1.00
D	—	—	—		1.00
6 yr old children					
A	0.99	0.99	1.00		1.00
B	—	0.94	0.92†	(0.92)*	0.99
C	—	—	0.98		1.00
D	—	—	—		1.00

* Predicted.

† Critical entry.

There is, however, one possible objection to our conclusion. In the training phase we showed the children the full length of the rods when we gave them feedback at the end of each trial. It is possible that the children solved the BD transitive question not by making a genuine transitive inference but simply by remembering that B was 6 inches and D was 4 inches. Such a solution to the problem is not an inferential one, and although we did not think that this kind of solution was likely, nevertheless we did not exclude its possibility in the first experiment.

We therefore carried out a second experiment on twenty-five 4 yr old and twenty-five 5 yr old children, in which our procedure was exactly the same as in the first experiment, except that we eliminated visual feedback during the training session. Instead of being shown which of the two rods was longer at the end of each training trial, the children were simply told which was the longer and which the shorter. The rods were never displayed completely until the whole experiment was finished.

The test results for this experiment are given in Table 2, which shows that the removal of visual feedback had no effect on children's ability to make transitive comparisons. Once again performance on all transitive comparisons was well above chance. The performance of both age groups was as good in the BD comparison in this experiment as the performance of the equivalent age groups in the first experiment. Again, however, the BD scores were somewhat lower than the BC and CD scores. We analysed the scores of the 4 and 5 yr olds on these three comparisons in the two experiments

Table 2 Probability of Correct Choices on Tests for Transitivity and Retention (Experiment 2)

Stimulus	B	C	D		E
4 yr old children					
A	0.98	0.98	0.93		0.97
B	—	0.89	0.82†	(0.77)*	0.90
C	—	—	0.87		0.88
D	—	—	—		0.94
5 yr old children					
A	0.98	0.92	0.95		0.97
B	—	0.87	0.85†	(0.85)*	0.98
C	—	—	0.97		0.95
D	—	—	—		0.98

* Predicted.

† Critical entry.

together, and again found a significant difference between pairs ($F_{3.89, d.f.2,172}, P < 0.05$). There was no interaction with age or with experiments. Thus in both experiments, children's transitivity, though considerable, was not perfect.

We shall now argue that the lower performance on the crucial BD pairs is not due to a failure to make inferences but to a failure of retention of the information contained in the initial comparisons. Let $P_{b,c}$ and $P_{c,d}$ be the respective probabilities

of recalling the information on the BC and CD pairs. Assume that the recall of these information units is independent. Then the probability of making a correct inference on the BD test ($P_{b,d}$) is the probability of jointly recalling the information for each of the training pairs. Since these events are independent, their probabilities multiply; that is, $P_{b,d} = P_{b,c} \times P_{c,d}$.

These assumptions were tested by multiplying the observed probabilities for the BC and CD tests for each subtable of Tables 1 and 2. The predicted $P_{b,d}$ is shown in parentheses. It can be seen that these predictions are reasonably close to the observed values. Hence, the lower performance on the BD tests may be attributed to a failure in memory rather than to inferential difficulty.

This last experiment conclusively demonstrates that very young children are able to make transitive inferences extremely effectively. They can combine separate quantity judgments very well and they can do so at a far younger age than has generally been assumed. This is a conclusion which has practical as well as theoretical importance.

Received June 18, 1971.

¹ Piaget, J., and Inhelder, B., *The Child's Conception of Space* (Routledge and Kegan Paul, London, 1956).

² Piaget, J., Inhelder, B., and Szeminska, A., *The Child's Conception of Geometry* (Routledge and Kegan Paul, London, 1960).

³ Smedslund, J., *Psychol. Bull.*, **71**, 237 (1969).

⁴ Flavell, J. H., and Wohlwill, J. F., in *Studies in Cognitive Development* (edit. by Elkind, D., and Flavell, J. H.) (Oxford University Press, New York, 1969).

Optimum $P\%$ Library of Scientific Periodicals

B. C. BROOKES

School of Library Archive and Information Studies, University College London, Gower Street, London WC1E 6BT

A quantitative method is described for finding the optimum percentage of periodicals for a library in a given field. The appearance of new journals is apparently counterbalanced by the disappearance of the old.

By applying two empirical laws of informatics it is now possible to design the most compact selection of scientific periodicals to cover any specified percentage $P\%$ of the total periodical coverage of any well defined scientific subject. The two laws are the Bradford law of scatter and the negative exponential law of obsolescence.

Ideal and Practical Totalities

If all scientific periodicals are supposed to be arranged in order of decreasing productivity of papers relevant to some specified subject S , an ordered linear array which can be subdivided into three exclusive sets is obtained.

The set S_1 consists of all periodicals which contribute an average of at least r papers/yr which are relevant to S . The

set S_2 consists of those periodicals which have contributed some papers relevant to S but with an average productivity which is less than r papers/yr. The set S_3 consists of those scientific periodicals which have not yet contributed papers relevant to S and are practically certain not to (Fig. 1).

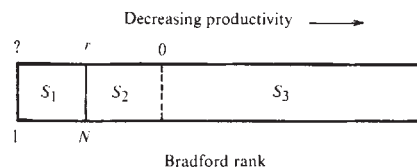


Fig. 1 The three sub-sets of periodicals.

From the point of view of a scientist interested only in the subject S , the periodicals of the set S_3 need not be identified. The periodicals of S_2 are identifiable by the fact that they have contributed some relevant papers: they must be regarded as candidates for inclusion in S_1 . The periodicals of set S_1 contain almost all the literature relevant to S if r is made small enough. To make quantitative analysis possible, some numerical value has to be assigned to r .

Bradford observed¹ that if the periodicals which contribute papers relevant to any well defined scientific subject S are

arranged in decreasing order of productivity and ranked 1, 2, 3, . . . , then the periodical ranks begin with a very productive "nuclear" zone (of ranks 1 to c , where c may be any number from 3 upwards and which increases with the generality of the subject) followed by a long tail of steadily less productive periodicals.

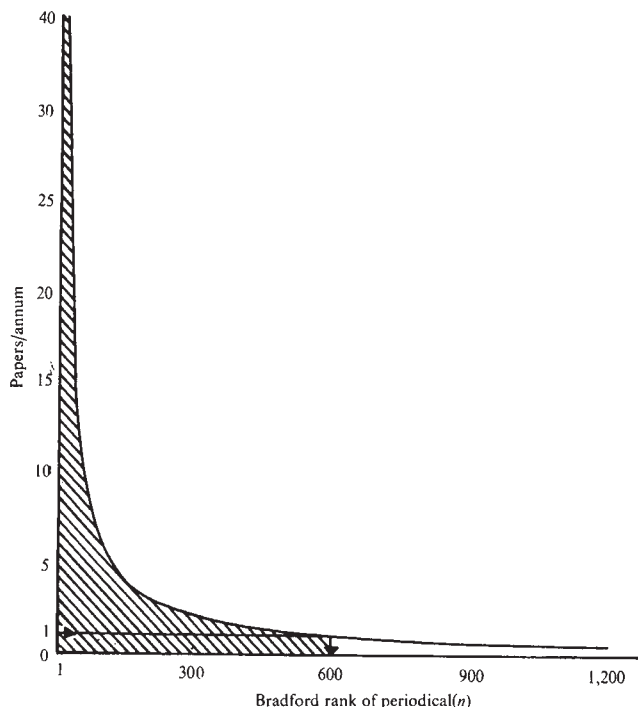


Fig. 2 The stipulated 100% totality (linear scales).

It has been shown² that the total number of relevant papers contributed by the periodicals of rank 1 to n is given by

$$R(n) = N \log_e n/s, (n \geq c) \quad (1)$$

where N is the number of periodicals which contribute an average of at least 1 paper/yr and s (> 1) is a constant characteristic of the subject. It follows that the periodical of rank n contributes N/n relevant papers/yr. The total number of papers contributed by set S_1 will therefore be

$$R(N/r) = N \log_e N/rs \quad (2)$$

When $n \leq N$ or $r \geq 1$, the contributing periodicals can all be identified without difficulty. When $n > N$, the periodicals contribute only occasionally and apparently at random.

For the purposes of this analysis it is therefore stipulated that the practical annual totality of papers relevant to S be that contributed by the periodicals ranked 1 to N , so that $r = 1$. This total, henceforward regarded as the 100% totality, is given by

$$R(N) = N \log_e N/s \quad (3)$$

For example, if $N = 600$, $s = 1.5$, then

$$R(N) = 600 \log_e 400 = 600 \times 5.99 \approx 3,600$$

Admittedly, this totality is arbitrarily defined; some further papers will be contributed by periodicals outside the set S_1 .

But any other definition of totality which is also quantifiable would be open to similar criticism. The difficulty is illustrated by Fig. 2 which shows how the annual productivity decreases as n increases up to and beyond N for the case in which $N = 600$, $s = 1.5$. The practical totality proposed is indicated by the shaded area.

Obsolescence

It is known that the immediate or scientific usage of scientific periodicals declines with the age of the periodical volumes. Strictly, this decline conforms closely with a negative exponential law but, in practice, because reference is usually given to the year of publication, it is much more convenient to use instead the geometric distribution:

$$p(t) = (1-a)a^{t-1}, (1 < t < \infty) \quad (4)$$

where $p(t)$ is the probability of reference to an issue of the periodical of age t years and a is a constant characteristic of the literature and of the nature of its usage.

It will be assumed that a is constant for all values of t . For $a < 1$, the series

$$1 + a + a^2 + \dots + a^{t-1} + \dots$$

converges to the sum $1/(1-a)$ as $t \rightarrow \infty$. If R references are made to a given periodical in a given library context during its first year of life, then aR references can be expected during its second year, a^2R references during its third year and so on. It is therefore possible to estimate the total number of references that will be made to it during its (infinite) lifetime. This total will be

$$R(1 + a + a^2 + \dots + a^{t-1} + \dots) = R/(1-a) \quad (5)$$

If the issue of the periodical is already t years old, then the number of further references to it that can be expected is given by

$$\begin{aligned} R(a^t + a^{t+1} + a^{t+2} + \dots) \\ = Ra^t(1 + a + a^2 + \dots) \\ = Ra^t/(1-a) \end{aligned} \quad (6)$$

which reduces to (5) when $t = 0$.

Within the given library context, expression (5) can be called the total utility of a periodical volume which has just been published; it will be denoted by $U(O)$. Its remaining utility at age t is given by (6) and can be denoted by $U(t)$. We then have

$$U(t) = Ra^t/(1-a) = a^t U(O) \quad (7)$$

For calculations on utilities the most convenient technique is to draw the graph of

$$a^t = U(t)/U(O) \quad (8)$$

using a logarithmic scale for $U(t)/U(O)$ (as a fraction or as a percentage) and a linear scale for t . Values of t corresponding to any fraction, for a given value of a , can then be read directly from the straight line graph, and vice versa.

The sum of the geometric series, $1/(1-a)$, decreases as a , the annual ageing factor, decreases; that is, short lived periodicals have a smaller total utility than periodicals in which interest declines more slowly. The factor $1/(1-a)$, which arises frequently in the analysis of obsolescence, will henceforward be called the utility factor of the periodicals and be denoted by u .

Application to a Bradford Periodical Set

It will now be assumed that all the relevant papers in the current issues of the set of N periodicals which constitute the totality are of equal significance. (It seems likely that the papers published in the periodicals of the nuclear zone are, on average, of greater significance than those in the more peripheral zones but this issue awaits empirical analysis.)

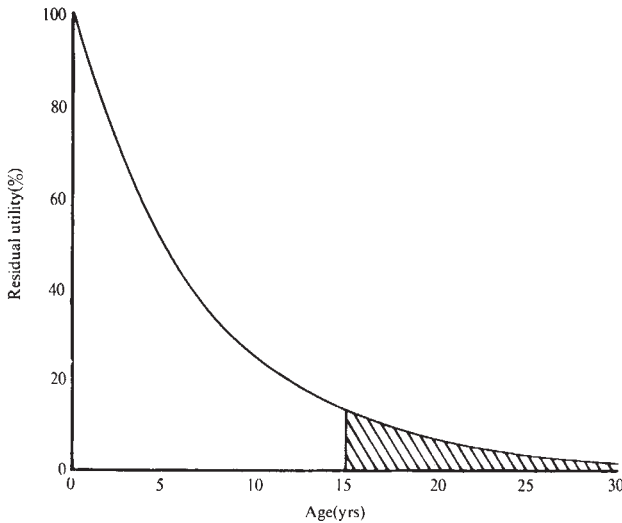


Fig. 3 The residual utility (linear scales).

Consider the utility of the periodical of rank n in a Bradford set. This periodical will have an annual average of N/n relevant papers and so the distribution of utilities over the successive years of its life from $t=0$ to $t=1, 2, \dots$ is given by the series

$$N/n (1 + a + a^2 + \dots + a^{t-1} + \dots) = Nu/n \quad (9)$$

$$\text{So its initial utility is } N/n \quad (10a)$$

$$\text{its utility at age } t \text{ is } N a^{t-1}/n \quad (10b)$$

$$\text{its total utility is } Nu/n \quad (10c)$$

$$\text{and its residual utility after } t \text{ yr is } Nua^t/n \quad (10d)$$

(These measures are relative rather than absolute, but it is not necessary to multiply each by the same constant when only comparisons within a given library context are being made.) We have so far regarded the series (9) as expressing the declining utility of a single volume of the periodical as it ages from $t=0$ to $t=1, 2, 3, \dots$ and so on (Fig. 3). But it can also be regarded as expressing the declining utilities of the ageing volumes of the periodical in its present complete run.

The sum of all the relevant papers in the Bradford set is given by

$$R(N) = N \log N/s$$

so that, for the complete Bradford set, the analogous utility measures are

$$\text{initial utility is } R(N) = N \log N/s \quad (11a)$$

$$\text{utility at age } t \text{ is } R(N)a^{t-1} = Na^{t-1} \log N/s \quad (11b)$$

$$\text{total utility is } R(N)u = uN \log N/s \quad (11c)$$

$$\text{and residual utility after } t \text{ years is } R(N)ua^t = uNa^t \log N/s \quad (11d)$$

We can now consider techniques of selecting $P\%$ of the total utility of a complete Bradford set of periodicals.

Some $P\%$ Solutions

There is an infinity of ways of selecting $P\%$ from the 100% totality. The simplest technique is to cut the complete Bradford set of N periodicals to the smaller set ranked $1, 2, \dots, M$, that is, to the M most productive periodicals. In this case M would be given by

$$N \log M/s = N \log N/s \times P/100$$

$$\text{so that} \quad M/s = (N/s)^{P/100} \quad (12)$$

For $N=600$, $s=1.5$, $P=50\%$ and 75% , this result yields $M=30$ for $p=50\%$ and $M=90$ for 75% (Fig. 4).

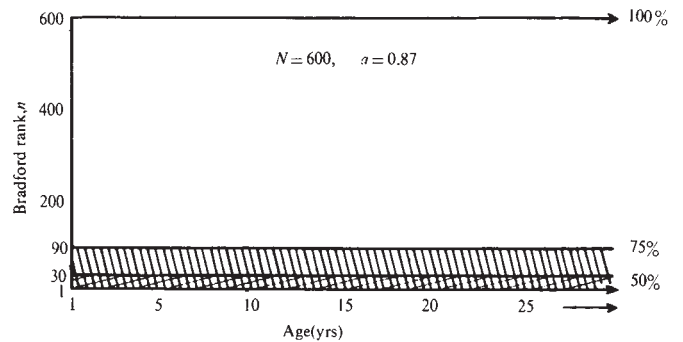


Fig. 4 The 50% and 75% "Bradford cut" solutions.

The solution reduces the expenditure on periodicals to the minimum for any specified value of P , but it has the disadvantage of leaving the shelves still occupied by the long little-used tails of the periodicals remaining so that the mean utility per metre shelf space is still low.

A second "cross cut" solution is to leave equal runs (in terms of years) on the shelves but to discard the ageing tails at the age given by

$$a^t = \frac{\text{discard utility}}{\text{initial utility}} = (1 - P/100) = f \quad (13)$$

For $a=0.87$ (half-life=5.0 yr) we have for $a^t=0.5$, $t=5.0$ yr and, for $a^t=0.75$, $t=10$ yr (Fig. 5).

Such solutions have the advantage of providing 100% coverage of papers published within some specified age limit, but the most productive periodicals are thus discarded when their residual utilities are still very high compared with the initial utilities of the peripheral periodicals.

A third solution, the "contour cut", is to discard tails of equal residual utility so that all the volumes remaining on the shelves have utilities above this critical discard level and yet give an overall $P\%$ coverage. This technique implies that

Table 1 Estimates of Shelf Space Required

Method	Bradford cut	Cross cut	Contour cut
50%	1,500	3,000	556
75%	4,500	6,000	2,570

Bradford set: $N=600$, $s=1.5$, $a=0.87$.

Shelf space is estimated in "periodical years", 100% required 30,000 periodical years for a 50 yr life.

periodicals of low initial utility will have much shorter runs than the more productive periodicals.

Consider the total loss of utility if the discard utility is equal to the initial utility of the periodical of rank M . We then have a discard utility level of N/M and for any periodical of rank n , where $c \leq n \leq M$, we have the age of discard, t , given by

$$a^t = \frac{\text{discard utility}}{\text{initial utility}} = \frac{N/M}{N/n} = \frac{n}{M} \quad (14)$$

The corresponding value of t can be read from the graph of a^t . The residual utility of the n th periodical at discard, using (10d) and (14), will therefore be

$$Nua^t/n = Nun/nM = Nu/M \quad (15)$$

Each of the M periodicals is, by this technique, discarding equal utilities, so the total utility thus discarded is Nu . Moreover, because the periodicals of rank $(M+1)$ to N have been discarded completely, we have the proportional loss of utility from the 100% totality, using (11c), given by

$$\frac{Nu + uN \log N/s - uN \log M/s}{uN \log N/s} = \frac{1 + \log N/M}{\log N/s} = f \quad (16)$$

from which the value of M for any specified value of f can be found. For $f=0.5$ and 0.25 and for the same numerical data used above, 50% utility would be provided by the most productive eighty-one periodicals and 75% utility by the most productive 364 periodicals when all are discarded as they decline to the same discard utility contours (Fig. 6). The technique is easy to apply because, when the contours are mapped on a graph on which n is logarithmic and t is linear, they appear as parallel straight lines for $c \leq n \leq N$.

Table 2 Costs per Relevant Paper

Range of set acquired	Yield of relevant papers per annum	Relative cost paper/yr
1-75	2,350	1
1-150	2,760	1.70
1-300	3,180	2.97
1-450	3,420	4.12
1-600	3,600	5.22

Bradford set: $N=600$, $s=1.5$.

The advantage of this contouring technique is that it provides the most compact solution of the $P\%$ library but costs more in the buying of periodicals than the Bradford cut method. (In practice it may be convenient or economical to use some hybrid form of two of these solutions but if the hybridization is rationally planned it is possible to estimate the corresponding

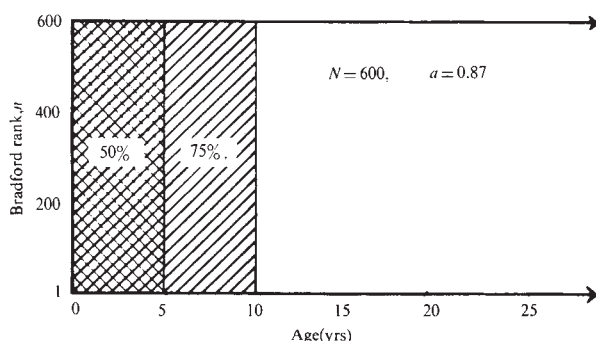


Fig. 5 The 50% and 75% "cross cut" solutions.

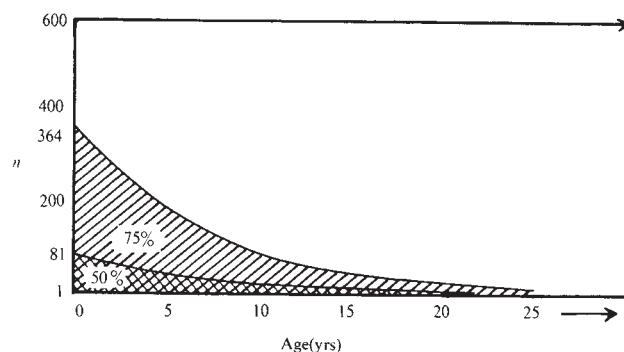


Fig. 6 The 50% and 75% "contour cut" solutions.

value of P for any compromise that may be decided on or to design the hybrid to conform with any specified value of P .)

Estimates of the shelf space demanded by each of the three solutions, in terms of "periodical years", are given in Table 1. In these estimates a complete back run is reckoned at 50 periodical years so that the 100% totality would require 30,000 periodical years. It can be seen that the contour method offers the most compact solutions.

Effects of Growth

The cost per relevant paper acquired by buying periodicals increases steadily as the range of the periodicals ranked 1 to n of a Bradford set increases (Table 2). It is therefore uneconomic to attempt 100% coverage especially if the particular science library is backed by some regional or national library serving many science libraries from which it can borrow periodicals, acquire photocopies or particular papers or receive suitable video transmissions. The cut-off point at which it becomes more economic to borrow than to buy³ then determines the value of P .

I have assumed that the literature of the particular scientific subject S grows uniformly year by year and that it conforms closely with the empirical laws applied. But even if these conditions are not fulfilled, the principles underlying the techniques can still be applied though more laborious graphical methods may have to be adopted. In practice, too, the Bradford set selected in any one year is also liable to change as new periodicals appear, as some die in their tracks and as others change the focus of their scientific interest. So once the required $P\%$ library has been established it will need regular review and revision. If the rate of growth of the literature is increasing, then the value of a can be expected to decrease from year to year. But increase in the rate of growth of the literature is more likely to arise from an increase in the number of scientific workers than from an increase in their output of scientific papers. An increase in the number of scientists working in the subject increases the utility of all the literature they depend on. And so the effects of the two kinds of growth act in opposite directions on the magnitude of a . It can be shown that if the two rates of increase are equal, then the value of a is unchanged⁴.

It is interesting that the $P\%$ library designed by the contour technique discards, year by year, as many annual volumes as it acquires. The "information explosion" becomes less alarming if it is appreciated that the "explosion" of new literature is almost exactly counterbalanced by the discarding of the old. But the librarian is conservative; he has yet to learn how to be as ruthless as his scientific colleagues in the art of discarding the obsolete.

Received January 29, 1971.

¹ Bradford, S. C., *Documentation* (London, 1948).

² Brookes, B. C., *Nature*, **224**, 935 (1969).

³ Brookes, B. C., *J. Doc.*, **26**, 22 (1970).

⁴ Oliver, M. R., *J. Doc.*, **27**, 11 (1971).

LETTERS TO NATURE

PHYSICAL SCIENCES

Solar Proton Medium Flux Constancy over a Million Years

THE data of cosmogenic radionuclide activity measurements in lunar material from the Apollo 11 and 12 missions have now been published¹⁻⁸. Unfortunately, the data concern chiefly the measurements of medium radioactivity of whole rock (by non-destructive gamma-spectrometry) or large volume samples (by radiochemical methods). The data provide no way to determine the overall depth distribution gradient of radionuclides, produced by galactic and solar cosmic rays, and so no information can be extracted about the intensity of cosmic rays. But ref. 1 describes how the radioactivities of some radionuclides have been measured as a function of depth in lunar sample 10,017. By analysing these data we have drawn a conclusion about possible constancy of solar proton medium flux for the last million years.

For our purpose the calculation of the depth distribution of cosmogenic isotopes in the surface layer of the Moon has been fulfilled, which allows accurate interpretation of the measurements. The calculation enables us to determine the distribution with depth of primary cosmic ray and secondary nuclear-active particles as well as the distributions of cosmogenic radionuclides⁹⁻¹¹. The efficiency of the method has been proved by numerous calculations of radioactivities in meteorites. Our calculations have been carried out for a large body ($d \ll R$) with composition similar to that of the lunar crystalline rock B/17-33/ (ref. 6), for which depth radioactivity was measured¹. The production cross sections of radionuclides from the different elements in the energy range 0.001 to 28 GeV have been taken from the experimental data of ref. 12. Unknown cross sections have been resolved from formulae (1) and (2) (*vide infra*) which link, by the ratios of Rudstam coefficients¹³, unknown production cross sections of an isotope from a target with experimental production cross sections of this isotope from other targets

$$\sigma_i^I(A_i Z_i) = \frac{K(A^I)}{K(A^{II})} \exp \{ [P(A^I) - P(A^{II})] A_i \} \sigma_i^{II}(A_i Z_i)^{\text{exper.}} \quad (1)$$

where I, II are the targets and i, j the isotopes, or, with that of other isotopes from the same target¹⁴

$$\sigma(A_i Z_i) = \exp [P(A_i - A_j) - R_i(Z_i - S A_i + T A_j^{2/3}) + R_j(Z_j - S A_j + T A_j^{2/3})] \sigma(A_j Z_j)^{\text{exper.}} \quad (2)$$

Thus, the same cross sections can be calculated from (1) and from (2) using different experimental data. The cross sections determined in this way were weighted according to the integral cosmic ray spectra and composition of the rock. The intensity and spectrum of the galactic cosmic rays were determined from the measurements in the stratosphere for the period 1958 to 1970 (refs. 15 and 16). The spectrum of solar protons with energy > 20 MeV has been given in ref. 17, together with depth distributions of solar protons and secondary neutrons

in the lunar surface layer. Because of the lack of data for the medium solar proton intensity over long periods of time we believe it is best for our purpose—to compare cosmic ray intensity for different time intervals—to determine the quantity of medium intensity solar protons by extrapolation of the measured activity data of one of the radionuclides (for example ^{22}Na) in lunar rock. Further calculations of the depth distributions of other radionuclides with different half lives, using the same value of solar proton intensity, will lead by comparison with measured activities of these isotopes to an estimate of the constancy of the solar proton flux.

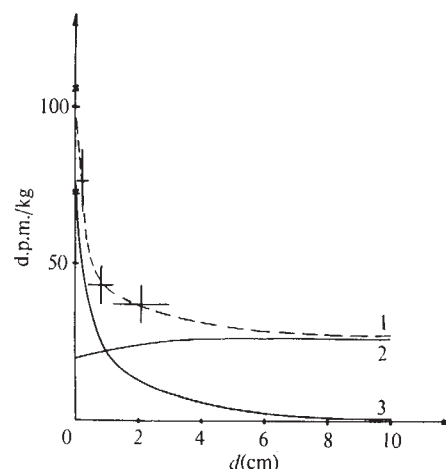


Fig. 1 Depth distribution of ^{22}Na radioactivity in the lunar rock B/17-33/. +, Measurement data from ref. 1; 1, extrapolation curve; x, extrapolation limits; 2, calculated ^{22}Na activity induced by galactic component of cosmic rays; 3, the difference between 1 and 2, showing the distribution of ^{22}Na activity, produced by solar protons; d , the distance from the lunar surface.

In Fig. 1 the ^{22}Na activity measured as a function of depth¹ is plotted, with experimental errors in the depth ranges marked. Extrapolation of curve 1 intercepts the ordinate at 96 d.p.m. kg^{-1} with $\begin{cases} +10\% \\ -25\% \end{cases}$ error (extrapolation limits marked by crosses on ordinate). Curve 2 shows our calculated depth distribution of ^{22}Na produced by the galactic component of cosmic ray and secondary nuclear-active particles. The difference between these curves (curve 3) shows accumulation of ^{22}Na by solar proton and secondary neutron bombardment. According to ref. 17 the secondary neutron flux is three orders of magnitude smaller than incident solar proton flux on the lunar surface, so that the interception point of curve 3 with the ordinate defines the activity induced by solar protons with intensity $2.46^{+0.44}_{-0.74}$ protons $\text{cm}^{-2} \text{ s}^{-1} \text{ sterad}^{-1}$ (that is, $\begin{cases} +18\% \\ -30\% \end{cases}$ error). This is the medium solar proton flux for 4 yr from 1966 to 1969 ($1.5 T_{1,2} \sim 4$ yr for ^{22}Na). With this value of medium intensity of solar protons the activities of other

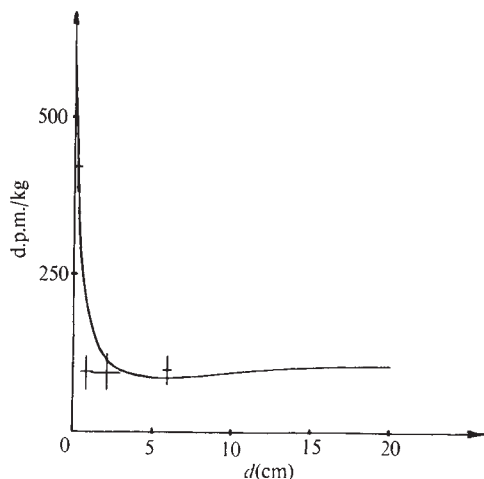


Fig. 2 Depth distribution of ^{55}Fe radioactivity in the rock B/17-33/.

long lived radionuclides in lunar rock B/17-33 have been calculated. In Fig. 2 the curve of calculated ^{55}Fe activity as a function of depth is plotted, with measured points from ref. 1. (The ^{55}Fe half life is the same as that of ^{22}Na .) In Fig. 3 the radioactivity data of ^{26}Al , with half life 7.4×10^5 yr, are plotted. The agreement between calculated (curve 1) and measured depth change of ^{26}Al activity is good. Extrapolation over ^{26}Al measured data, in the same way as for ^{22}Na above, gives medium solar proton intensity $2.46^{+0.34}_{-0.54}$ protons cm^{-2}

$\text{s}^{-1} \text{sterad}^{-1}$ (that is, $\begin{cases} +14\% \\ -26\% \end{cases}$ error). We have also calculated the depth distributions of ^{26}Al activity induced by solar protons with twice smaller intensity (curve 2) and with twice greater intensity (curve 3). For depth $d > 4$ cm all three curves draw nearer because of the fall in solar proton flux, but the corresponding ^{26}Al activities on the surface lie far outside the limits of possible extrapolation.

It follows from this analysis that at least within $\sim 30\%$ error we can say that the mean intensity of solar cosmic rays

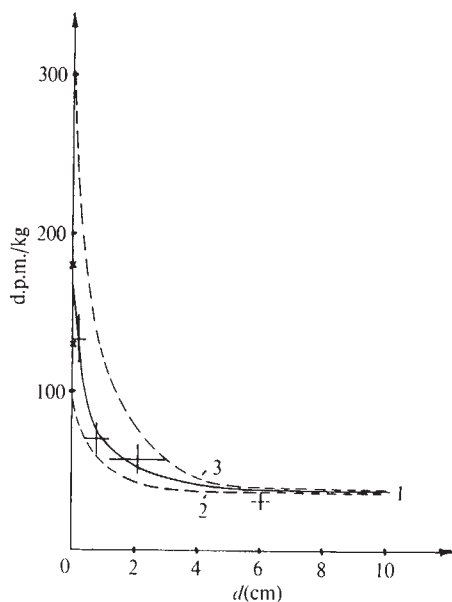


Fig. 3 Depth distribution of ^{26}Al in the rock B/17-33/. +, Measurement data from ref. 1; 1, ^{26}Al activity calculated using the medium solar proton intensity $31.1 \text{ protons cm}^{-2} \text{s}^{-1}$; 2, depth distribution of ^{26}Al , calculated with twice smaller solar proton flux; 3, ^{26}Al distribution, calculated with twice greater solar proton flux; x, the limits of possible extrapolation.

with the energy $> 20 \text{ MeV}$ has been constant for the last million years at about $31.1^{+5.6}_{-9.4}$ protons $\text{cm}^{-2} \text{s}^{-1}$. This conclusion is confirmed by calculations of radioactivities of ^{53}Mn ($T_{1/2} = 2 \times 10^6 \text{ yr}$) and ^{54}Mn ($T_{1/2} = 303 \text{ d}$).

A. K. LAVRUKHINA
G. K. USTINOVA

Vernadsky Institute of Geochemistry and
Analytical Chemistry,
Academy of Sciences of the USSR, Moscow

Received April 6, 1971.

- Shedlovsky, T. P., Honda, M., Reedy, R. C., Evans, J. C., Lal, D., Lindstrom, R. M., Delany, A. C., Arnold, J. R., Loosli, H., Fruchter, J. S., and Finkel, R. C., *Science*, **167**, 574 (1970).
- Perkins, R. W., Rancitelli, L. A., Cooper, J. A., Kaye, J. H., and Wogman, N. A., *Science*, **167**, 577 (1970).
- O'Kelley, G. D. O., Eldridge, J. S., Schonfeld, E., and Bell, P. R., *Science*, **167**, 580 (1970).
- Fireman, E. L., D'Amico, J. C. D., and DeFelice, J. C., *Science*, **167**, 566 (1970).
- Stoerner, R. W., Lyman, W. J., and Davis, R., *Science*, **167**, 553 (1970).
- Wanke, H., Begemann, F., Vilcsek, E., Rieder, R., Tescka, F., Born, W., Quijano-Rico, M., Voshage, H., and Wlotzka, F., *Science*, **167**, 523 (1970).
- Lunar Sample Preliminary Examination Team: Apollo-11, *Science*, **165**, 1211 (1969).
- Preliminary Examination of Lunar Samples from Apollo-12, *Science*, **167**, 1325 (1970).
- Lavrukhina, A. K., and Ustinova, G. K., *Astronomicheskij Zh.*, **44**, 1081 (1967).
- Lavrukhina, A. K., and Ustinova, G. K., *Dokl. Acad. Sci. USSR*, **179**, 1448 (1968).
- Lavrukhina, A. K., Ustinova, G. K., Ibraev, T. A., and Kuznetsova, R. I., *Meteorite Research*, 227 (Reidel, Dordrecht, 1969).
- Bruninx, E., *High-Energy Nuclear Reaction Cross-Sections*, I-III, CERN 64-17, Nucl. Phys. Div., Geneva, 1961, 1962, 1964.
- Rudstam, G., *Z. Naturforsch.*, **21a**, 1027 (1966).
- Lavrukhina, A. K., and Ustinova, G. K., *Izvest. Acad. Sci. USSR*, **34**, 2401 (1970).
- Charachchjan, A. N., and Charachchjan, T. N., *Trans. Sixth All-Union Winter School on Cosmic Phys.*, Part II, 36 (Apatity, 1969).
- Bazilevskaya, G. A., Kvashnin, A. N., Svirzevskaya, A. K., Stozkov, Ju. I., Charachchjan, A. N., and Charachchjan, T. N., *The Report on All-Union Conf. on Cosmic Rays* (Moscow, 1970).
- Ebeoglu, D. B., and Wainio, K. M., *J. Geophys. Res.*, **71**, 5863 (1966).

Extragalactic Faraday Rotation

IN three very important and groundbreaking papers, Sofue, Fujimoto and Kawabata¹, Kawabata *et al.*², and Reinhardt and Thiel³ call attention to evidence which indicates that Faraday rotation is taking place in space outside our own Galaxy. Essentially they show that above low galactic latitudes, where material in the disk of our own Galaxy is known to produce Faraday rotation, extragalactic radio sources exhibit Faraday rotations which generally increase with the redshift of the source, and that these rotations behave similarly in certain regions of the sky.

They attribute this extragalactic Faraday rotation to a metagalactic magnetic field which is ordered on the scale of the observable universe (the scale observable on the assumption that the redshifts of the quasars are cosmological). It seems to me, however, reasoning in analogy with our own Galaxy, that this latter model is not the most likely one with which to explain the extragalactic Faraday rotations. It would not, for example, be logical to look to the low-density polar regions and possible ordered magnetic field in our own Galaxy for Faraday rotation. Instead we look to the plane where we know there are concentrations of ionized matter and magnetic

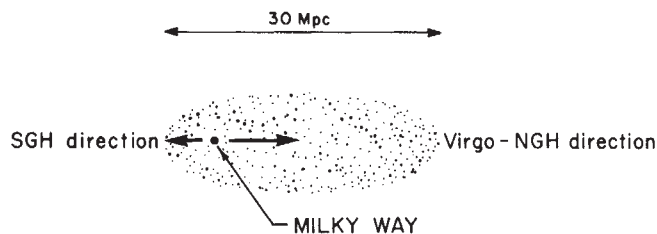


Fig. 1 Schematic cross-section of the local supercluster showing location of Local Group and approximate dimensions.

field in the form of gas, H II regions, and spiral arms. In fact, this is where the galactic Faraday rotation is observed.

When we look outside our own Galaxy, however, we see something analogous in the local supercluster of galaxies as outlined by de Vaucouleurs⁴. In that supercluster there is a concentration of galaxies in the supergalactic plane. Those galaxies represent the concentrations of ionized matter and magnetic field which we know about—and it is here that the authors of refs. 1–3 find the maximum extragalactic Faraday rotation.

That direction of maximum Faraday rotation was designated originally by Sofue *et al.* as $l^{\text{II}} = 100^\circ$, $b^{\text{II}} = -30^\circ$ and the opposite direction in the sky $l^{\text{II}} = 280^\circ$, $b^{\text{II}} = 30^\circ$. In the latest paper by Kawabata *et al.*, the direction is designated as $l^{\text{II}} = 115^\circ$, $b^{\text{II}} = -5^\circ$. Perhaps this difference is an indication of the uncertainty of the determination. In any case, as Sakashita and Kaneko pointed out², this direction lies in the plane of the supercluster. It is close to the direction of the Virgo cluster $l^{\text{II}} = 280$ to 300 , $b^{\text{II}} = +50$ to $+70$, which marks the approximate centre of the local supercluster as seen from our own Galaxy.

In order to test further the alternatives represented by the two models, we should indicate that the local supercluster is supposed to be a flattened system of galaxies and clusters of galaxies about 30 Mpc in diameter, as shown in Fig. 1. Our own Local Group of galaxies is located somewhere out near the edge, so that we see the bulk of the supercluster in the direction of Virgo, but there is also a lesser amount of supercluster which we look out through in the opposite direction.

objects is about 0.1 greater in the supercluster centre direction as opposed to the supercluster anticentre direction. I have previously suggested that most quasars and quasarlike compact galaxies are at distances closer than their redshifts would indicate⁵ and are, in fact, generally members of the Local Group and local supercluster. In that case we would expect more distant quasars, on the average, in the direction of the bulk of the supercluster and fewer lower-redshift objects in the anticentre direction. This kind of distribution would be expected to give Faraday rotation from material within the local supercluster roughly as indicated in Table 1.

Finally, it is necessary to test the increase in the mean absolute value of the Faraday rotation as a function of the redshift of the source. None of the previous papers have shown such a plot, but Fig. 2 shows the Faraday rotations for high-latitude radio sources as a function of redshift. Although there is considerable scatter, it is clear that the sources with very low redshifts have $\langle |RM| \rangle \sim 10$ rad/m², the sources with $z \sim 0.5$ have $\langle |RM| \rangle$ between 10 and 20, and the sources with $z \sim 1.0$ have $\langle |RM| \rangle \sim 30$. I agree with the previous authors² that there is a general rise in the mean absolute value of the Faraday rotation with increasing redshift. But a most important result now appears after redshifts of about $z = 1.2$. The five quasars with redshifts $z \sim 2$ definitely have $\langle |RM| \rangle \sim 10$ rad/m² again. Kawabata *et al.* seem to explain this as arising from a disordered metagalactic magnetic field which dominates beyond a distance which corresponds to a redshift (cosmological) of about $z = 1.4$. But on their picture, regardless of how disordered the field is outside $z = 1.4$, the radiation must traverse the region between $z = 1.4$ and the observer, and it should therefore be rotated by at least the ~ 30 rad/m² in that region. Although there are few data available they certainly indicate, using this model, that the $z \sim 2$ quasars are closer than the $z \sim 1$ quasars and are in fact at distances corresponding to the $z \sim 0.1$ to 0.3 quasarlike objects.

This last result seems particularly significant because the evidence discussed earlier⁵ indicated that the quasars with redshifts of the order of $z = 0.2$ are low-luminosity Local Group objects, and that with higher redshifts the quasars become of higher luminosity and generally distributed throughout the local supercluster of galaxies. But for redshifts around $z \sim 2$ the evidence indicated that they are once again low-luminosity objects distributed in space in the Local Group and nearby regions of the supercluster.

It is interesting to note from Table 1 that the Faraday rotations in the north galactic hemisphere are about evenly divided between plus and minus. We would conclude that this occurs as the radiation encounters concentrations of plasma in the local supercluster which have no preferred alignment. On the other hand, the ten Faraday rotations in the south

Table 1 Faraday Rotations for Sources with $b^{\text{II}} > 42^\circ$, $0.1 < z < 1.2$

North Galactic Hemisphere			South Galactic Hemisphere		
Source	z	RM	Source	z	RM
1353+19	0.72	+7	2115-30	0.98	+28
1328+254	1.06	-60	2135-14	0.20	+19
1545+21	0.26	+20	2313+03	0.22	+7
1622+23	0.93	+31	2309+09	0.23	+3
3C286	0.85	+4	0035-02	0.22	+1
3C254	0.73	-23	0056-00	0.72	-1
3C219	0.17	-10	0159-11	0.67	+4
1040+12	1.03	+31	0336-01	0.85	+23
1127-14	1.19	+31	0350-07	0.96	+23
1136-13	0.55	-22	0403-13	0.57	+4
1229-02	0.39	+19	$\langle z \rangle = 0.56 \pm 0.06$ (p.e.)		
1241+16	0.56	-18	$\langle RM \rangle = 11.3 \pm 2.1$ (p.e.)		
1253-05	0.54	+24			
1335-06	0.63	-13			
1330+02	0.22	+2			
$\langle z \rangle = 0.66 \pm 0.05$ (p.e.)					
$\langle RM \rangle = 21.0 \pm 2.4$ (p.e.)					

Data from Reinhardt and Thiel, Table 1. (Note their value of b^{II} for 3C390 should be changed from $+60$ to $+6$.) 3C273 is excluded from this table as anomalous.

Table 1 shows that the Faraday rotations in the north galactic hemisphere (the general direction of the centre of the supercluster) average about twice the absolute value of Faraday rotations in the direction of the south galactic hemisphere (opposite the centre of the supercluster). Another interesting result is that the mean value of the redshifts of these quasars and allied

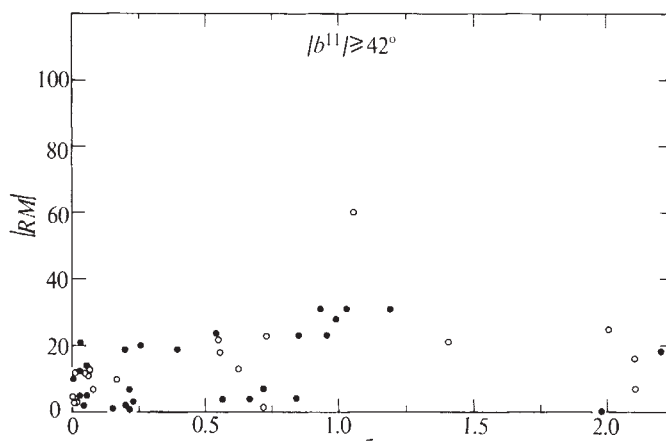


Fig. 2 Plot of Faraday rotation (●, positive; ○, negative) against redshift of source. Data from Reinhardt and Thiel, Table 1.

galactic hemisphere are almost all at least slightly positive. This may indicate there is some preferential alignment of magnetic field within our own Local Group of galaxies, the centre of which lies in the direction of M31 in the south galactic hemisphere. An additional point can be made about the quasars with very high redshifts. Of the seventeen quasars with redshifts greater than $z=1.5$ known in 1968, thirteen lie in the south galactic hemisphere. This would support the inference that they are Local Group objects concentrated in the general direction of M31.

Finally, it can be remarked that the previous authors¹⁻³ estimated a mean electron-density-magnetic-field component of $n_e B_{||} \sim 10^{-14}$ along the path length to quasars if they were at their cosmological distances. If I use a distance on the average of 1/100 of this for the quasars, an $n_e B_{||} \sim 10^{-12}$ would be derived for the local supercluster. Because we are dealing with the same order of extragalactic Faraday rotation as galactic, we can scale the observed galactic Faraday rotation near the plane in our own Galaxy (about 300 pc path length with $n_e B_{||} \sim 10^{-7}$ to 10^{-8} gauss/cm³) to the scale of the supercluster (about 30 Mpc). This yields $n_e B_{||} \sim 10^{-12}$ to 10^{-13} , in agreement with the observations for the supercluster. This mean value of $n_e B_{||}$ is reasonable, so the question arises of how might it be distributed along the line of sight. It must be between the two extremes of completely even, homogeneous spatial distribution and complete concentration into regions the size of the optical diameters of galaxies. If we indeed have some intermediate distribution of this Faraday rotating plasma—say on the scale of groups or clusters of galaxies—then we would expect the radio emission from quasars and compact galaxies to intersect regions of higher and lower $n_e B_{||}$ as it crosses the supercluster, and suffer Faraday rotations of either plus or minus sense with an increasing dispersion as the distance across the supercluster increases.

HALTON ARP

Hale Observatories,
Carnegie Institution of Washington,
California Institute of Technology,
Pasadena, California 91101

Received May 28, 1971.

¹ Sofue, Y., Fujimoto, M., and Kawabata, K., *Publ. Astron. Soc. Japan*, **20**, 368 (1969).

² Kawabata, K., Fujimoto, M., Sofue, Y., and Fukui, M., *Publ. Astron. Soc. Japan*, **21**, 293 (1969).

³ Reinhardt, M., and Thiel, M., *Astrophys. Lett.*, **7**, 101 (1970).

⁴ Vaucouleurs, G. de, *Soviet A. J.*, **3**, 897 (1959).

⁵ Arp, H., *Astron. J.*, **75**, 1 (1969).

Evidence for Black Holes in Binary Star Systems

ONE of the most exciting predictions of the general theory of relativity is that a star of more than about $1.4 M_{\odot}$ may undergo gravitational collapse to produce a black hole when it has exhausted its nuclear fuel. It would therefore be a very important confirmation of the theory if such holes could be detected. Unfortunately their very small size (a few km) makes it virtually impossible to observe them directly, but their existence could be inferred from the motion of other objects in their gravitational field. The natural place to look for black holes therefore is in binary star systems in which only one object is observed (single line binaries). Thorne and Trimble¹ gave a list of all single line spectroscopic binaries in Batten's² catalogue in which the mass of the unseen object was estimated to be $1.4 M_{\odot}$ or over. In most of these binaries the unseen secondary was less massive than the primary observed star and therefore could have been a normal star which is not observed in comparison with its brighter com-

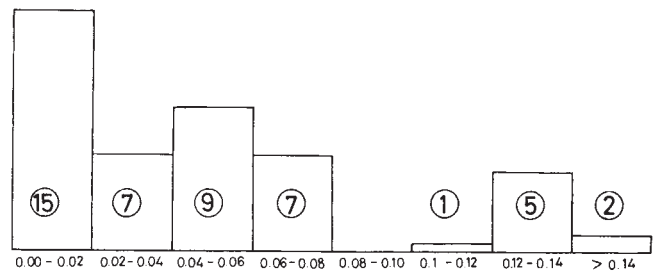


Fig. 1 The eccentricities of forty-six short period double line spectroscopic binary systems.

panion. In a smaller number of cases the secondary was heavier than the primary, but in each of these cases Trimble and Thorne were able to suggest a possible reason why it might not have been observed. They concluded therefore that while some of these single line binaries might contain black holes there was no compelling reason for believing that any of them did.

Here we would like to present an additional argument not considered by Trimble and Thorne. This suggests that at least one or two of these binaries may contain black holes. The evidence for this comes from studying the eccentricities of the shortest period binaries.

In a short period binary system (say, with a period of less than 5 days) one would expect any initial eccentricity of the orbits to be damped out. This is because of dissipation processes such as tidal friction, mass exchange and magnetic breaking which will reduce the energy of the system but not its angular momentum. The orbit therefore tends to that with the lowest energy for a given angular momentum, that is, a circular orbit. Suppose now that one of the stars collapses to form a black hole. Then in a time short compared with the orbital period it might lose a significant fraction of its mass by the emission of gravitational waves or the ejection of a shell of matter. In addition, in unpublished work by one of us (S. W. H.), it is shown that in the Brans-Dicke theory the object will lose the fraction of its mass which arises from the scalar interaction ($\sim 7\%$). This sudden mass loss will cause the orbit which was initially nearly circular to acquire an

eccentricity of $e = \frac{\Delta M_2}{M_1 + M_2}$ where M_1 and M_2 are the final

masses of the two stars and ΔM_2 is the mass loss of the second star. This eccentricity will eventually be damped away but at a rather slower rate because tidal dissipation will occur only in the star which has not collapsed. It will be observable if the collapse did not occur too long ago.

To test this idea we have compared the eccentricities of short period double line binaries—that is, binaries where both stars are observed—with those of short period single line binaries. We examined all the binaries in Batten's catalogue² with a period less than 5 days and where the masses of both objects were above $1.4 M_{\odot}$ and where the quality of the data was not considered bad (class *a* to *d* in Batten's classification). In the case of the double line binaries we excluded those eleven where the eccentricity was assumed zero. In fact these probably have very low eccentricities. The distribution of eccentricities for double line binaries is shown in Fig. 1. From this it can be seen that most of them (38 out of 46) have very low eccentricities (below 0.08). There are eight binaries with eccentricities above 0.08. Seven of these have spectral types B3 or earlier and are probably younger than 10^8 yr. This indicates that the damping time for loss of eccentricity is probably of the order of 10^8 yr in a close binary. The eighth binary is exceptional in that its spectral type is AO which is considerably later and its eccentricity is 0.29 whereas the next highest eccentricity is 0.19. This spectroscopic binary is in fact one visual component of the visual double system γ Andromeda (ADS

Table 1 Single Line Binaries ($M_1, M_{2\min} \geq 1.4 M_\odot$, Period < 5 days) (taken from ref. 1)

No. in Batten's catalogue	Star	α_{1900}	δ_{1900}	Magnitude	Spectral type	Period	e	$f(M)$	$M_1/M_\odot$	$M_{2\min}/M_\odot$
195	HD 40005	05 h 51.1 m	+16° 21'	6.91	B3V	3.036	0.0	0.157	10.0	3.0
544	HD 176318	18 h 54.6 m	+38° 07'	5.70	B6V	2.912225	0.169	0.150	5.0	1.9
567	201 G Sgr	19 h 27.3 m	-40° 15'	5.9	A3III	4.625	0.09	0.180	3.0	1.6
596	HD 191473	20 h 05.0 m	+36° 57'	8.6	B0.5V	4.2876	0.0447	0.535	15.0	6.2
617	HD 194495	20 h 20.8 m	+21° 10'	7.09	B7	4.9052	0.133	0.275	6.0	2.8
634	HD 198754	20 h 47.6 m	+37° 36'	6.97	B3	3.30353	0.018	0.082	10.0	2.3
683	HD 209961	22 h 02.0 m	+47° 45'	6.27	B2V	2.1721	0.0	0.47	12.0	5.2

1630). The other visual component of this system has a highly eccentric orbit which at periastron will pass fairly close to the spectroscopic binary. At each close passage it will be likely to change the eccentricity of the binary by a small amount. In 10^8 yr there will be more than a million such passages and so the present observed eccentricity could have been produced by a random walk process.

Table 1 shows all single spectroscopic binaries in Batten's catalogue which have periods less than 5 days and where Trimble and Thorne estimated that the masses of each object were greater than $1.4 M_\odot$. They estimated the mass, M_1 , of the primary from its spectral type and then obtained a lower limit on the mass M_2 of the secondary from the observationally determined quantity $f(M) = M_2 \sin^3 i / (M_1 + M_2)^2$ where i is the angle between the line of sight and the normal to the plane of the orbit. Of the seven systems in this table one (HD 209961) has an eccentricity which was assumed to be zero. Of the remainder three (HD 176318, 201 G Sgr and HD 194495) have eccentricities greater than 0.08. On the basis of seven double line binaries out of forty-six with high eccentricities one would expect three or more out of a sample of seven with a probability of less than 8%. This is suggestive but it is not good enough for one to be confident that one or more of these binaries contains a black hole. But there is some supporting evidence for the black hole hypothesis in the fact that, whereas in the case of the double line binaries those with high eccentricities are among the earliest in spectral type, those single line binaries with high eccentricities are all distinctly later and are not among the earliest types in their class. We therefore suggest that it would be worth examining these three binary systems more carefully to see whether one could rule out the possibility that the secondary was a normal star which has not been observed to date because it is less luminous than the primary. In the case of 201 G Sgr the primary is a giant and so overluminous for its mass; one could therefore not hope to detect the secondary in this system; however, in HD 176318 and HD 194495 the secondaries, if they are normal stars, should be less than 3.4 and 2.7 magnitudes respectively down on the primaries. With the use of image intensifiers it might be possible to detect them. It might also be worth looking for these objects in other wave bands—Zel'dovich and Guseynov⁵, for example, have pointed out that matter falling into a black hole could cause the emission of X-rays.

In 201 G Sgr and HD 176318 the lower limits on the mass of the secondary are just below the highest estimates of the maximum mass of neutron stars⁶. It is therefore just possible that these two could be neutron stars. In the case of HD 194495, however, the lower limit on the mass of the secondary is $2.8 M_\odot$ which is too high to be a neutron star. If the present observed eccentricities of these systems resulted from mass loss,

$$\frac{\Delta M_2}{M_2 + \Delta M_2}$$

would be less than 0.39 for HD 176318, 0.21 for 201 G Sgr and 0.29 for HD 194495.

To summarize, there is suggestive but not conclusive evidence for the presence of black holes in binaries. The evidence could be strengthened by careful observations which

could rule out the possibility that the secondaries in these binaries are normal stars.

We thank Dr Virginia Trimble for help and advice.

G. W. GIBBONS

*Department of Applied Mathematics and
Theoretical Physics,
University of Cambridge*

S. W. HAWKING

*Institute of Theoretical Astronomy,
University of Cambridge*

Received June 30, 1971.

- Trimble, V. L., and Thorne, K. S., *Astrophys. J.*, **156**, 1013 (1969).
- Batten, A. H., *Pub. Dom. Astrophys. Obs. Victoria*, **13**, 119 (1967).
- Maestre, L. A., and Wright, J. A., *Astrophys. J.*, **131**, 119 (1960).
- Muller, P., *J. des Observateurs*, **40**, 48 (1957).
- Zel'dovich, Ya. B., and Guseynov, O. H., *Astrophys. J.*, **144**, 841 (1965).
- Tsuruta, S., "The Effects of Nuclear Forces on the Maximum Mass of Neutron Stars" in *The Crab Nebula* (edit. by Davies, R. D., and Smith, F. G.) (Reidel, Dordrecht, in the press).

Arctic Palaeotemperatures in Late Caenozoic Time

RECONSTRUCTION of the climatic and hydrologic history of ocean basins has been based on either oxygen isotope palaeothermometry or studies of foraminiferal assemblages preserved in deep sea sediments. We report here the application of both methods to deep sea sediments collected from the Arctic Ocean by the Lamont-Doherty Geological Observatory. Oxygen isotope determinations were made on two selected cores from the central Arctic basin to test the validity of the palaeoceanographic interpretations based on microfaunal analysis¹⁻³. Details of the cores are given in Fig. 1 and Table 1. Analyses of the cores have already been published in detail: here we wish to summarize what we have discovered about the history of the Arctic Ocean¹⁻⁴.

Biostratigraphic and lithologic correlations between cores accompanied by $^{18}\text{O}/^{16}\text{O}$ determinations and radiometric

Table 1 Location, Depth and Length of Cores

Core	Latitude	Longitude	Depth	Length
D.st.A.2	83° 52' N	168° 12' W	1,521	206
D.st.A.3	84° 12' N	168° 33' W	2,409	95
D.st.A.4	84° 21' N	168° 49' W	2,041	116
D.st.A.5	84° 28' N	169° 04' W	1,934	125
D.st.A.6	85° 15' N	167° 54' W	1,842	88
Arlis II, 1	81° 57' N	168° 07' E	2,816	44
Arlis II, 2	82° 00' N	168° 04' E	2,864	80
T3-67-4	79° 22.7'	174° 46'	1,760	272
T3-67-9	79° 37.9'	172° 07'	2,237	356
T3-67-11	79° 34.9'	172° 30'	2,810	250
T3-67-12	80° 21.9'	173° 33'	2,867	374

dating were used to estimate ages and sedimentation rates as well as to reconstruct the climatic and oceanographic history of the Arctic^{3,4}. The time interval of the longest core (T3-67-12, Fig. 3) is thought to exceed 3.3 m.y. Ages were estimated by interpolations and extrapolations based on radioisotope determinations⁵ and close interval faunal and lithologic correlations with neighbouring cores that have an established palaeomagnetic stratigraphy. Age assessments have been modified from those presented in a previous publication³, due to reinterpretation of the palaeomagnetic data of core 224 by Clark and his colleagues⁶. The earlier palaeomagnetic ages^{7,8} had apparently been greatly over-estimated.

On the basis of faunal and sediment characteristics three climatic units can be distinguished. The oldest, unit III, was deposited between about 3.3 m.y. and 3 m.y. ago; it consists of foraminifera-poor, Fe and Mn oxide-rich sediments. Calcareous foraminifera, in part corroded, are thick shelled forms. Arenaceous foraminifera (*Glomospira gordialis*, *Cyclammina pusilla* and *Alveolophragmium subglobosum*) dominate the benthic assemblages. Lower than present sedimentation rates could account for the selective solution of the less resistant limy tests and impoverished character of the fauna.

Unit II was deposited between approximately 3 and 0.7 m.y. ago and is poor in both Fe, Mn oxides and in foraminifera. It contains one foraminifera-rich layer: the predominant foraminifer in this layer is temperate-arctic, euryhaline *Globigerina quinqueloba* (¹⁸O/¹⁶O determinations). This species occurs with sinistral *Globigerina pachyderma* throughout unit II. Fragile calcareous benthonic foraminifera (*Stetsonia horvathi*, *Sphaerodina bulloides* and *Bolivina arctica*) periodically abound, constituting up to 88% of the fauna. Concentration of thin walled benthonic foraminifera suggests that the near absence of plank-

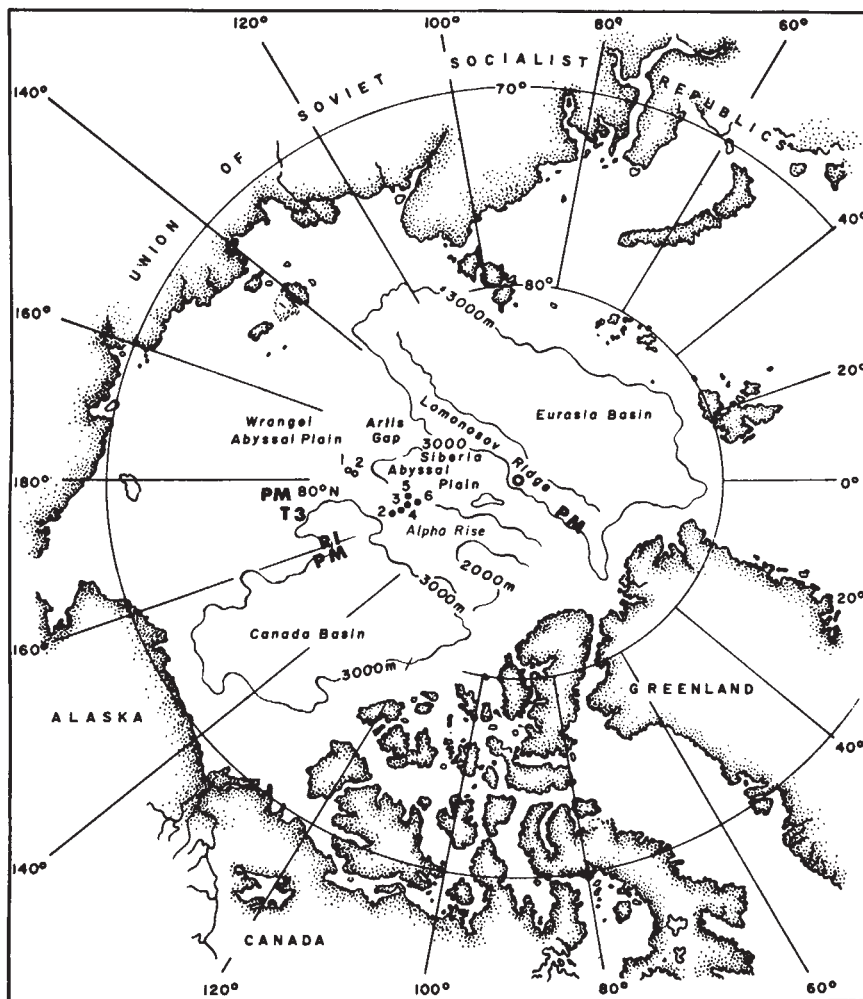
tonic forms was due to adverse environmental conditions rather than to dissolution of the less resistant tests. It has been suggested that the Arctic was essentially free of permanent pack ice during the deposition of units II and III (refs. 2, 3).

Unit I was deposited in the past 0.7 m.y., a time of conspicuous climatic fluctuations as indicated by the temporal variations in fauna and in mineral/fauna ratio (Fig. 2 and Fig. 3). Beds rich in both foraminifera and in Mn, Fe oxides alternate with layers poor in both foraminifera and Mn, Fe oxides. The former represent conditions similar to present (permanent pack ice cover) and contain sinistral *G. pachyderma* almost exclusively^{3,4}. *G. quinqueloba* attained high frequencies at the beginning and end of some of these cold periods. In the foraminifera-poor beds, sinistral *G. pachyderma* is accompanied by *G. quinqueloba*. Pteropods (*Limacina helicina*) are preserved principally in core tops. Unit II/unit I boundary approximately corresponds to the last major polarity reversal in the Earth's magnetic field conveniently marking the Brunhes/Matuyama boundary³. Ice rafted debris throughout the cores indicates that high latitude glaciation commenced before 3.3 m.y. ago.

Among the factors determining surface water salinity in the Arctic, precipitation, evaporation, ocean currents, convective mixing and the presence of drift ice are considered most important and the oxygen isotopic composition of Arctic surface water is determined by the same factors⁹. Evaporation results in concentration of ¹⁸O while precipitation and river inflow cause its dilution. The range of present day surface water temperature and salinity is -1.6° C to 0° C and <29‰-33‰ respectively¹⁰.

As a result of slow vertical mixing, present day surface salinities are about 4.8‰ lower than those of the bottom water¹⁰. Analysis of ¹⁸O/¹⁶O for Arctic water¹¹ indicates that the ¹⁸O

Fig. 1 Bathymetric map of the Arctic Ocean based on the geological map of the Arctic (1960). T3 shows the location of cores T3-67-4,9,11,12 while PM shows the location of cores with known palaeomagnetic stratigraphy and RI locates the radioisotopically dated core. Dark and light circles show location of previously studied cores¹⁻³.



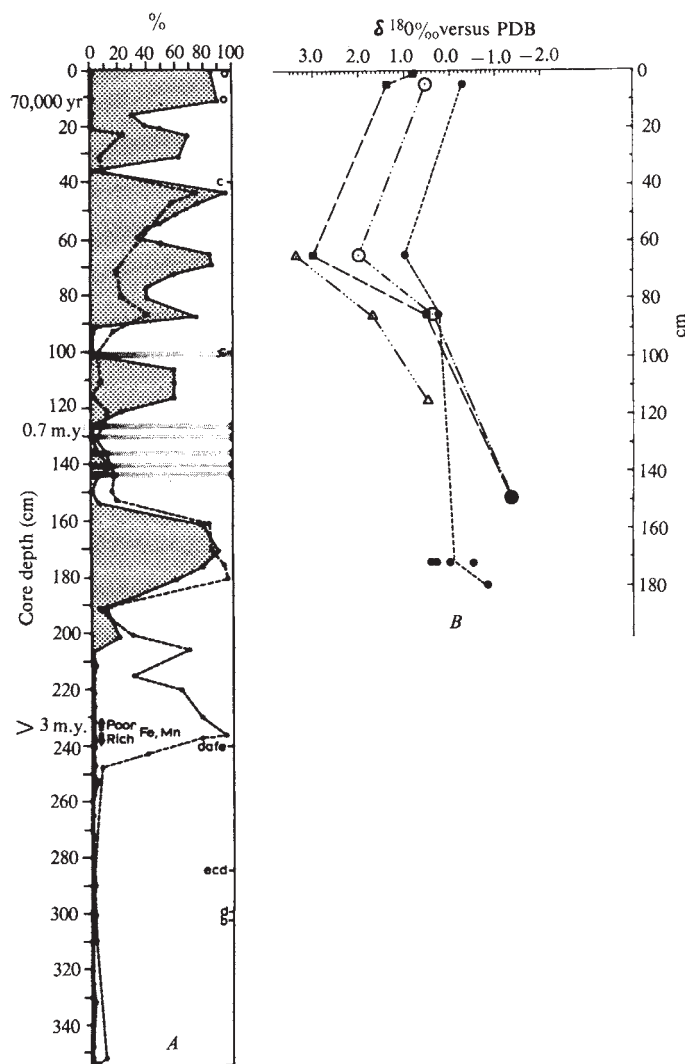


Fig. 2 Core T3-67-9. *A*, Variation of microfauna to clastics in the coarse fraction ($>62\ \mu\text{m}$). The shaded areas represent volume percentages of microfauna. The occurrence of low latitude foraminifers is as follows: *a*, *Globorotalia menardii*—*tumida*; *b*, *Globorotalia scitula*; *c*, *Globorotalia* sp.; *d*, *Globigerinoides* sp.; *e*, *Globigerinoides ruber*; and *f*, *Sphaeroidinella dehiscens*. The circles represent pteropods and the dashed line gives the percentage of *G. quinqueloba* complex out of the total planktonic population. Dark horizontal lines are horizons where benthonic foraminifers are in excess of 10%. *B*, The variation in $\delta^{18}\text{O}$ for: ■, *G. pachyderma*; ●, *G. quinqueloba*; ○, average planktonic species; and △, total planktonic and benthonic foraminifers.

depletion closely follows the salinity profile, with $\delta^{18}\text{O}$ changing by 0.8‰ with 1‰ change in salinity in the upper 350 m. This surface seawater is depleted in ^{18}O by about 4‰ , while at greater depth $\delta^{18}\text{O}$ approaches values close to SMOW.

The $^{18}\text{O}/^{16}\text{O}$ ratios of calcareous tests from foraminifera-rich and foraminifera-poor layers were determined (Figs. 2 and 3). The measurements were made on an Atlas-Werke M86 mass spectrometer developed by Nier. The foraminifers were hand picked, and treated with commercial 'Clorox' solution; the CO_2 was extracted from the CaCO_3 according to the method described by McCrea¹².

To calculate the temperatures from the $^{18}\text{O}/^{16}\text{O}$, the formula of Epstein *et al.*¹³, modified by Craig¹⁴, was used

$$t = 16.9 - 4.2(\delta_s - \delta_w) + 0.13(\delta_s - \delta_w)^2$$

The established relation

$$\left(\delta_s^{18}\text{O} = \frac{^{18}\text{O}/^{16}\text{O} \text{ sample}}{^{18}\text{O}/^{16}\text{O} \text{ standard}} - 1 \times 1,000 \right)$$

depends on the water temperature ($t^\circ\text{C}$) as well as on the iso-

topic composition of the water in which the organisms lived.

When sufficient shell material was available, planktonic tests were analysed separately from the benthonic forms. Moreover, when samples yielded adequate amounts of the two dominant planktonic foraminifers, *G. quinqueloba* and *G. pachyderma*, their tests were analysed separately. As indicated in Figs. 2 and 3 the former registered consistently lower $\delta^{18}\text{O}$ values than the latter. This can readily be explained by their differing life habitats: *G. quinqueloba*, an epiplanktonic form, incorporates the CaCO_3 necessary for test building at surface, in the isotopically lighter, low salinity water, whereas the thick shelled *G. pachyderma*, known to inhabit greater water depth¹⁵, constructs the early part of its shell at surface, and the outer, thick cortex at greater depth, in denser, more saline water, hence its great $^{18}\text{O}/^{16}\text{O}$ value. Determinations of $\delta^{18}\text{O}$ made on composite samples of benthonic and planktonic foraminifers indicate that, with one exception, the bottom water was enriched in ^{18}O (Figs. 2 and 3) attesting to the restricted vertical mixing and subsequent density stratification of the Arctic water.

As mentioned previously, changes in the $\delta^{18}\text{O}$ of the seawater are reflected in the oxygen isotopic ratios of the calcareous foraminiferal tests. The greatest shift towards positive values occurs at 65 cm depth in core T3-67-9 and at 40 cm depth in core T3-67-12 (Figs. 2 and 3); both samples come from foraminifera-rich horizons and were deposited during a period when seawater was colder and/or more saline than today.

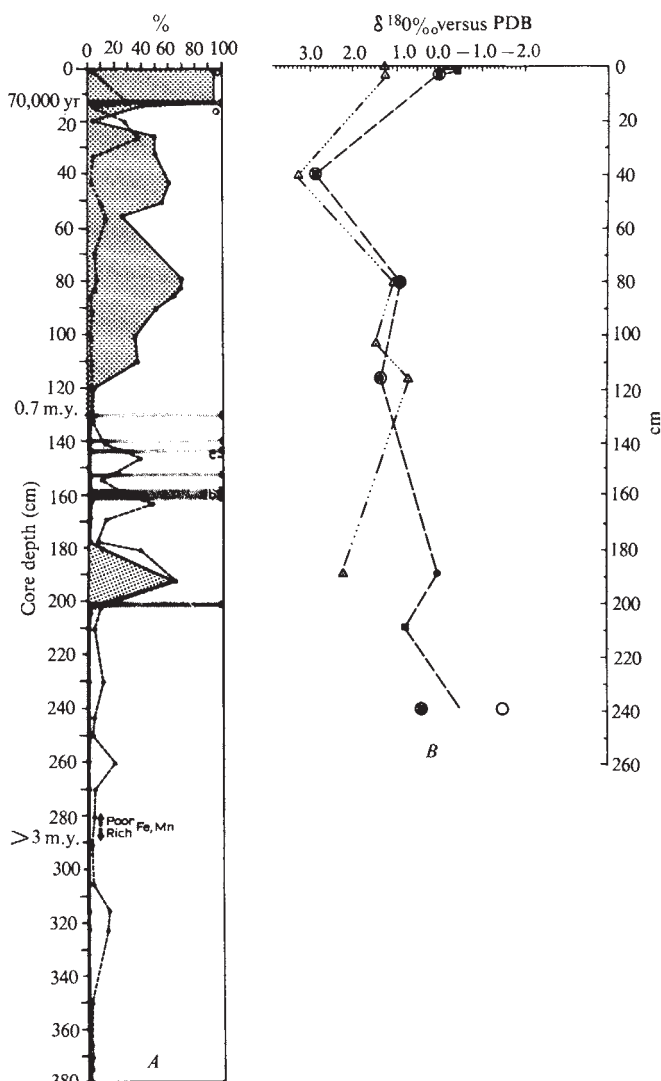


Fig. 3 Core T3-67-12. *A*, Variation in microfauna to clastics. Same legend as for Fig. 2. *B*, Variation in $\delta^{18}\text{O}$. Same legend as for Fig. 2.

Below 85 cm $\delta^{18}\text{O}$ values are more negative than in the core "tops" suggesting slightly warmer and/or less saline water in the Arctic basin between 3.3 and 0.7 m.y. ago than those of the present.

In conclusion, oxygen isotope and palaeontological determinations of planktonic foraminifers allow us to make several generalizations on the palaeoceanographic history of the Arctic Ocean back to Mid Pliocene. We conclude that the surface and deep water underwent periodic fluctuations and that the average surface water temperatures have varied between about -2°C and $+0.5^\circ\text{C}$, with salinities ranging from approximately 36‰ to <29 ‰, during the time interval represented by the cores investigated. This assumption is based on the $^{18}\text{O}/^{16}\text{O}$ data combined with the estimated environmental requirements of the extant planktonic foraminiferal species¹⁵.

Temperature minima correspond to the upper Pleistocene, probably the Riss (Illinoian) or Würm (Wisconsin) Glacial, whereas higher temperatures and/or lowest salinities were registered by foraminifers between about 3.3 million and 0.7 million years BP.

We thank P. E. Rosenberg and J. R. O'Neil for valuable suggestions, K. Hunkins for collecting the cores and R. Capo for shipping the samples. Coring operation was supported by ONR and NSF grants to Lamont-Doherty Geological Observatory.

YVONNE HERMAN

Department of Geology,
Washington State University,
Pullman, Washington 99163

C. VERGNAUD GRAZZINI

Université de Paris,
Faculté des Sciences,
Laboratoire de Géologie Dynamique et Centres,
de Recherches Géodynamiques,
Paris

C. HOOPER

Department of Geology,
Washington State University,
Pullman, Washington 99163

Received May 3, 1971.

- ¹ Herman, Y., *Nature*, **201**, 386 (1964).
- ² Herman, Y., *Palaeogeog.*, *Palaeoclimatol.*, *Palaeoecol.*, **5**, 251 (1969).
- ³ Herman, Y., *Science*, **169**, 474 (1970).
- ⁴ Herman, Y., *Second Intern. Symp. on Arctic Geol.*, San Francisco, Abstr., 25 (1971).
- ⁵ Ku, T. L., and Broecker, W. S., *Prog. Oceanog.*, **4**, 105 (1967).
- ⁶ Clark, D. L., *Geol. Soc. Amer. Bull.*, **81**, 3139 (1970).
- ⁷ Clark, D. L., *Arctic*, **22**, 233 (1969).
- ⁸ Steurwald, B. A., Clark, D. L., and Andrew, J. A., *Earth Planet. Sci. Lett.*, **5**, 79 (1968).
- ⁹ Craig, H., and Gordon, L. I., *Symp. in Marine Geochem.*, **3**, 277 (1965).
- ¹⁰ Treshnikov, A. F., *Intern. Oceanog. Cong.*, New York, Abstr., 522 (1959).
- ¹¹ Van Donk, J., and Mathieu, G., *J. Geophys. Res.*, **74**, 3396 (1969).
- ¹² McCrea, J. M., *J. Chem. Phys.*, **18**, 849 (1950).
- ¹³ Epstein, S., Buchsbaum, R., Lowenstam, H., and Urey, H. C., *Geol. Soc. Amer. Bull.*, **64**, 1315 (1953).
- ¹⁴ Craig, H., *Stable Isotopes in Oceanog. Studies and Palaeotemp.*, Spoleto (1965).
- ¹⁵ Boltovskoy, E., *Micropalaeontol.*, **15**, 237 (1969).

Palaeoclimatic Significance of the Stagnation of the Cariaco Trench

ALMOST all available information about the past thermal behaviour of the oceans has been obtained by studying the oxygen isotope ratios of cores from the deep sea¹. One basic limitation of that method is that to derive a palaeotemperature curve from oxygen isotope data one must assume some initial

value for the oxygen isotope ratio in the ocean at the time each sample was formed. There has been little independent evidence of past oceanic temperatures to provide a check on these assumed values, and some questions have been raised² about the significance of the $^{16}\text{O}/^{18}\text{O}$ palaeotemperature record. I suggest that the deep water of the Cariaco Trench may provide an estimate of the late glacial surface temperature of the Caribbean Sea which is completely independent of the oxygen isotope method.

The Cariaco Trench is a small closed basin off the coast of Venezuela with a sill depth of about 146 m and a maximum depth of 1,400 m^{3,4}. The water in the trench is presently anaerobic below a depth of 375 m and isothermal below 250 m, but sediment cores indicate that during late glacial time the bottom of the trench was ventilated and that the present stagnant condition developed about 10,900 radiocarbon years ago^{4,5-7}.

I suggest that during the late glacial period of ventilation of the deep waters of the Cariaco Trench, oceanic cooling and overturning enabled oxygenated surface waters to descend to the bottom of the trench; the isothermal and isohaline conditions must then have extended to the surface, because of vigorous mixing. These conditions ended when surficial warming at the beginning of the postglacial established a stable stratification; the deep water of the trench has been isolated since that time. I therefore regard the deep water as "fossil" late glacial age surface water in some respects. In particular, the deep water can hardly have cooled since the late glacial, because the overlying water is warmer than the deep water, and the geothermal heat flux prevents loss of heat downwards. Therefore, I regard the present deep water temperature of 16.9°C as the maximum possible surface temperature for the waters of the Cariaco Trench at the end of the last glaciation. This is in contrast to the modern values of 24°C to 26°C (ref. 3), and implies a temperature difference of at least 7°C between the late glacial period and the present.

This interpretation provides an unusual opportunity to check some of the assumptions which must be made in oxygen isotope work.

DAVID P. ADAM

Laboratory of Tree Ring Research,
University of Arizona,
Tucson, Arizona 85721

Received May 3, 1971.

- ¹ Emiliani, C., *Science*, **171**, 571 (1971).
- ² Shackleton, N., *Nature*, **218**, 79 (1968).
- ³ Richards, F. A., and Vaccaro, R. F., *Deep Sea Res.*, **3**, 214 (1956).
- ⁴ Lidz, L. L., Charm, W. B., Ball, M. M., and Valdes, S., *Bull. Marine Sci. Gulf Caribbean*, **19**, 1 (1969).
- ⁵ Broecker, W. S., Ewing, M., and Heezen, B. C., *Amer. J. Sci.*, **258**, 429 (1960).
- ⁶ Heezen, B. C., Menzies, R. J., Broecker, W. S., and Ewing, M., *Bull. Geol. Soc. Amer.*, **69**, 1579 (1958).
- ⁷ Athearn, W. D., *Woods Hole Oceanog. Inst. Tech. Rep.*, 65-37 (1965).

Monolithic Light Emitting Diode Arrays using Gallium Phosphide

THE high diode packing densities that can be achieved on single crystal slices of semiconductors mean that monolithic arrays of light emitters offer the possibility of displaying typescript signed characters from a 7×5 matrix, either for direct visual applications or for data recording. Previously this has only been achieved using the direct band gap semiconductors gallium arsenide and gallium arsenide phosphide, which emit radiation in the infrared or extreme red parts of the spectrum. Two problems have prevented gallium phosphide being used in monolithic arrays; they are the low electrolumin-

escent efficiencies obtained from junctions formed by diffusion into indirect band gap materials and the lack of an adequate mask for use on gallium phosphide to define the diode areas during gaseous zinc diffusion.

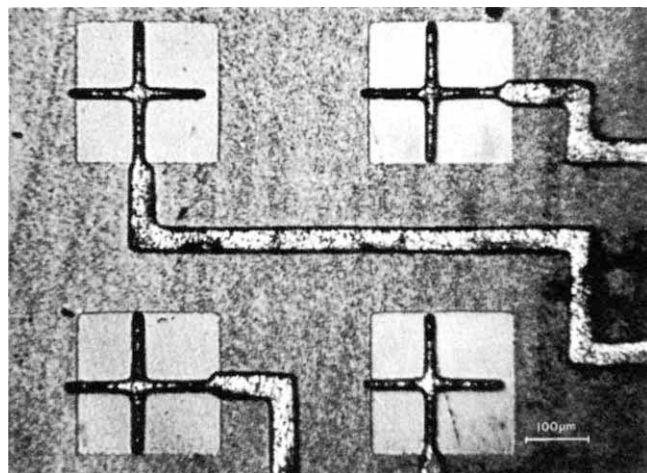


Fig. 1 Photograph of four diodes in a monolithic array. The diode squares are light emitting zinc diffused areas, the remainder of the surface being covered by the dielectric mask. Contact is made to the devices by aluminium interconnectors, the cross structure being used on top of the diode to facilitate current spreading.

We have fabricated green emitting monolithic arrays from epitaxial layers of gallium phosphide grown from gallium solution onto substrates cut from ingots produced by the liquid encapsulated Czochralski process¹ or grown by the vapour transport method². These layers were doped with sulphur so as to have a carrier concentration in the range $5 \times 10^{16} - 10^{17} \text{ cm}^{-3}$ and had nitrogen added so as to give a concentration in the semiconductor of approximately $2 \times 10^{18} \text{ atoms cm}^{-3}$. The nitrogen substitutes for the phosphorous atom in the lattice, so acting as a shallow trap which is responsible for the green emission process³. In order to produce a p-n junction we have then diffused zinc into the layer at 650°C resulting in a surface zinc concentration of $3 \times 10^{18} \text{ atoms cm}^{-3}$. The relatively low zinc level produced in the material enables the conditions for good electroluminescent efficiencies in an indirect band gap material to be established. The diode areas have been defined by diffusing through holes cut by photolithographic techniques in a triple mask of silica, silicon nitride and silica. This structure has excellent adhesion to the gallium phosphide and also has a low porosity to zinc atoms, so enabling it to act as an effective diffusion mask.

The monolithic arrays produced by this process have had electroluminescent efficiencies for green emission up to 0.1% at a current density of 20 A cm^{-2} . This compares with the best reported figure of 0.35% for individual diodes produced by the more complex double liquid epitaxial process grown on Czochralski substrates⁴.

This work was carried out in part under a CVD contract and is published by permission of the UK Ministry of Defence (Navy Department).

M. A. CARTER
A. MOTTRAM
A. R. PEAKER
P. D. SUDLOW
T. WHITE

Ferranti Ltd,
Chadderton,
Lancashire

Received June 7, 1971.

- ¹ Bass, S. J., and Oliver, P. E., *J. Crystal Growth*, **3**, 4, 286 (1968).
- ² Mottram, A., Peaker, A. R., and Sudlow, P. D., *J. Electrochem. Soc.*, **118**, 318 (1971).
- ³ Dean, P. J., Gershenzon, M., and Kaminsky, G., *J. App. Phys.*, **38**, 5332 (1967).
- ⁴ Logan, R. A., White, H. G., and Wiegmann, W., *Solid State Electron.*, **14**, 55 (1971).

Drag Reduction arising from Adhesive Tapes

COSSAR has reported¹ that the presence of a uniform layer of double-sided adhesive tape ('Scotch' brand) on the floor of a water channel can have a significant influence on the mean-velocity profile in the boundary layer of a turbulent flow. Indeed, Cossar's experiments indicate that, in his operating conditions, the velocity distribution above a layer of adhesive tape is almost the same as that obtained in flow over rough boundaries for which the mean height of roughness is about 0.040 inches (0.116 cm). He accordingly suggested that 'Scotch' tape is physically "sticky" towards water. But Cossar's interpretation of his results is open to question: it may be that, rather than increasing the resistance to the flow, the influence of the adhesive tape reduces it. This conclusion can in fact be inferred from Cossar's results. For flows past smooth boundaries, the shear stress τ exerted on the boundary is related to the viscosity η and the normal velocity gradient by

$$\tau = \eta \left(\frac{\partial u}{\partial y} \right)_{\text{wall}} \quad (1)$$

where u is the tangential velocity and y is the normal coordinate. But this is a good approximation only for boundaries that are hydraulically smooth, in the sense that the surface irregularities lie within the viscous sublayer of the flow. If, on the other hand, the roughness elements at the boundary are large enough, they can contribute to the shear stress exerted on the boundary through an effective form drag (see ref. 2, page 376), and then equation (1) is invalid. Indeed, it is usual for values of $\partial u / \partial y$ near the wall to decrease as the surface roughness increases (compare Cossar's results), although the actual shear stress exerted on the boundary increases. If we now make the assumption that the adhesive tape in Cossar's experiments was hydraulically smooth, it follows that the observed reduction in $\partial u / \partial y$ —which presumably extends right up to the wall—is accompanied by a reduction in shear stress, compared with what it would be on a smooth insoluble wall.

If these conclusions are correct they might have some interesting implications, for it would seem that the drastic changes in flow properties observed by Cossar emanate from the absorption into solution of some adhesive from the tape. But the solubility in water of the gum of such adhesive tapes is rather low, which suggests that only extremely small quantities of additive are needed to change the structure of the turbulent boundary layer, provided the additive is supplied in "sensitive" areas.

Naturally these ideas are speculative. To check them some solutions of adhesive were made by soaking pieces of tape in water, and then the drag reduction properties of these solutions were measured in turbulent pipe flows.

The apparatus used consisted of a hypodermic syringe to which a 93 cm length of hypodermic tubing of 1 mm bore was attached. The syringe was filled with the solution to be tested, and a known pressure was applied to the plunger of the syringe, forcing the liquid through the small-bore tubing. An electronic counter was used to measure the time for a given quantity of liquid (usually 10 ml.) to be ejected. The ejection times determined in this way were easily reproducible, for a given fluid, to within $\pm 2\%$. The drag reduction was taken

BIOLOGICAL SCIENCES

Quantitative Evidence for Protein Denaturation as the Cause of Thermal Death

THE specific cause of the death rates of unicellular organisms and poikilothermic animals at high temperatures is not known for certain¹. We wish to report a good numerical correlation between certain thermodynamic parameters in protein denaturation and death rates, where these have been reported, for these organisms. A similar correlation may exist between the thermal denaturation of other biopolymers, such as DNA and RNA, and thermal death, but in the absence of adequate data we cannot consider this possibility further.

At sufficiently high temperatures (>315 K) most proteins denature with pseudo-first order kinetics. This implies that the renaturation rate is slow enough to be negligible, and the rate is described by $dn/dt = -k_D n$. The first order denaturation rate constant, k_D , varies exponentially with temperature and is usually described by the absolute rate theory equation²

$$k_D = \kappa \frac{k_B T}{h} \exp[\Delta S^\ddagger/R] \times \exp[-\Delta H^\ddagger/RT] \quad (1)$$

where $\Delta S^\ddagger$ and $\Delta H^\ddagger$ are the activation entropy and activation enthalpy respectively.

We have found evidence from the work of Williams and Milby³ on the thermal denaturation of rhodopsins that, for the proteins tested, the $\Delta S^\ddagger$ and $\Delta H^\ddagger$ values were related by the simple linear equation⁴

$$\Delta S^\ddagger = a\Delta H^\ddagger + b \quad (2)$$

The existence of such a relationship constitutes a compensation law behaviour, because variations of $\Delta H^\ddagger$ in the negative exponential of equation (1) are partially compensated by parallel variations of $\Delta S^\ddagger$ in the positive exponential in their effects on k_D . (At the temperature $T = 1/a$, the compensation is exact and the denaturation rate is independent of the values of $\Delta H^\ddagger$ and $\Delta S^\ddagger$. This temperature, T_c , is the compensation law temperature.) Such compensation law behaviour occurs in a number of physical and chemical processes⁵⁻⁹ for which *ad hoc* explanations have been suggested. So far there is no compelling evidence that such a rule as equation (2) can be derived from general thermodynamic principles. Exner¹⁰ has pointed out that, in certain limited conditions, a compensation law may occur accidentally, and he has provided a set of criteria for judging the reliability of the rule. In some of the cases described here, such criteria have been used and satisfied.

We tested the generality of such a compensation law using the compilation of thermodynamic data on protein denaturations from Joly¹¹. Fig. 1 presents all these data, plotted as $\Delta S^\ddagger$ versus $\Delta H^\ddagger$, with no selection. All the data cluster about a linear regression line. From a least squares fit of the data points, the line yields a value of $T_c (= 1/a)$ of 329 K and a value of $b = -64.9$ calories/mol $\times$ K (an equally valid intercept could be the value of $\Delta H^\ddagger$ when $\Delta S^\ddagger = 0$; this yields $\Delta H^\ddagger = 21.3$ kcal/mol). The corresponding values for the rhodopsins are: $T_c = 334$ K and $b = -66$ calories/mol $\times$ K. Several of the proteins are represented by a number of points, each referring to a specific pH or ionic strength of the solution. Therefore, although the $\Delta S^\ddagger$ and $\Delta H^\ddagger$ values for a given protein may vary depending on the experimental conditions, the values always fall on the same line.

Sukhorukov and Likhtenshtein¹² have published a plot similar to Fig. 1 for a large number of proteins, which overlap only partially the proteins of our figure. The values we have estimated from their plot are: $T_c \approx 325$ K, $b \approx -70$ calories/mol $\times$ K, which are closely similar to ours. They have also included proteins and viruses in the dry state, as well as proteins in alcohol-water mixtures, and in D₂O solution, all of which still fall on the compensation law line.

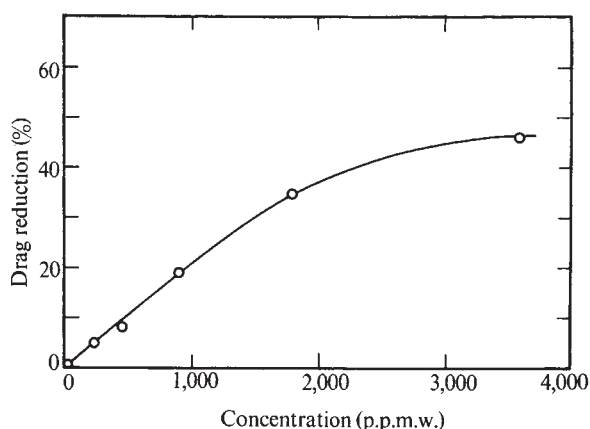


Fig. 1 Drag reduction of a solution of 'Scotch' tape in petroleum ether. Solvent Reynolds number was 60,000.

to be the fractional increase in the flow rate of the sample over that obtained for the solvent alone.

In view of Cossar's results it was initially anticipated that an extremely dilute solution, obtained from soaking 'Scotch' tape in water, would give rise to a large drag reduction. But early attempts to observe the Toms effect with such solutions proved unfruitful, and it was only after prolonged soaking of the tape that any effect was observed. For example, after soaking 0.02 m² of 'Scotch' tape in 200 ml. of water for 40 days, the resulting solution showed a drag reduction of 19% compared with water when ejected at a Reynolds number of 8,200. With another proprietary brand of adhesive tape ('Sellotape') the same procedure gave a drag reduction of 8% which rose to 20% after 80 days of immersion. In connexion with these measurements it is perhaps worth noting that: (i) the viscosity of the 'Scotch'-tape solution, measured under laminar flow conditions, was about 6% greater than that of water at the same temperature; and (ii) the drag reduction remained unchanged when the adhesive tape solutions were passed through filter paper (Whatman No. 1 grade) before being tested.

To obtain a solution of known concentration, the gum from a sample of 'Scotch' tape was completely dissolved in a "good" solvent (petroleum ether). The properties of this solution are not expected to differ greatly from those of the corresponding aqueous solution. The values of the drag reduction obtained at various dilutions are shown in Fig. 1. At a concentration of 3,600 p.p.m.w., when the viscosity of the solution was 50% greater than that of the solvent, the drag reduction was 46%. The results in Fig. 1 suggest that, compared with some drag reducing compounds, the concentrations of the present solutions need to be quite large in order to produce substantial drag reduction. On the other hand, if our suggestions regarding Cossar's experiments are correct, it would seem from his results that only extremely small quantities of additive can have large influences on a turbulent boundary layer when it is supplied from the wall. Accordingly it might be highly effective, for drag reduction, to coat surfaces with such compounds, which, because of their poor solubility in water, could have a fairly long period of effectiveness.

B. J. S. BARNARD
W. G. PRITCHARD

Fluid Mechanics Research Institute,
University of Essex

Received June 25, 1971.

¹ Cossar, A. E., *Nature*, **227**, 1044 (1970).

² Goldstein, S., *Modern Developments in Fluid Dynamics* (Clarendon Press, Oxford, 1938).

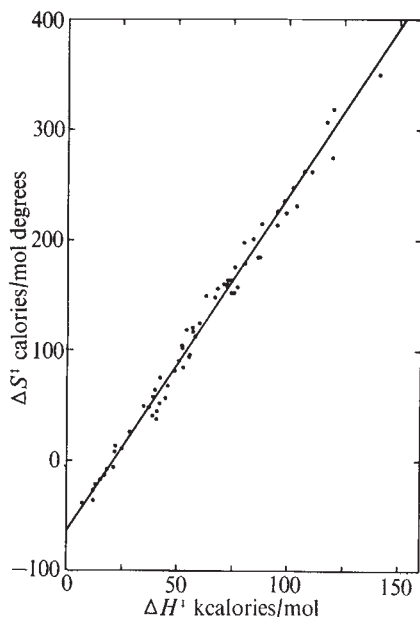


Fig. 1 A plot of the activation entropy, $\Delta S^\ddagger$, versus the activation enthalpy, $\Delta H^\ddagger$, for protein denaturation (after Joly¹¹). The regression line is a least squares fit to the data, and the close clustering to the line indicates the validity of the compensation law (equation 2). The constants of the line are: $T_c = 329$ K, and $b = -64.9$ calories/mol $\times$ K.

We conclude that virtually all proteins⁷, in a variety of conditions, denature at elevated temperatures according to the compensation law of equation (2), with the same value of T_c and b .

Lumry (personal communication) has called our attention to the work of van Uden and his co-workers¹³ who have reported compensation law behaviour in the thermal killing of yeasts. Here again (1) the death rates followed pseudo-first order kinetics with respect to time; (2) the specific thermal death rate, k_D , depended exponentially on temperature; and (3) the $\Delta S^\ddagger$ and $\Delta H^\ddagger$ values obtained were correlated according to equation (2). From their data we have calculated the values of the compensation law constants as $T_c = 325$ K and $b = -64.5$ calories/mol $\times$ K.

We have attempted to pursue this correlation with other unicellular organisms such as viruses and bacteria. Usable data in the literature are surprisingly scant, but Barnes *et al.*¹⁴ have carefully investigated this compensation law in the thermal inactivation of the Sindbis virus. Their data again meet the three criteria described above, and they calculate $T_c = 330$ K; while we calculate $b = -64$ calories/mol $\times$ K. In the case of bacteria, data are available on *Pseudomonas fragi*¹⁵, *Staphylococcus aureus*^{16,17}, and two strains of *Salmonella*¹⁷ which also meet our three criteria. The values we have calculated for the compensation law constants are $T_c = 331$ K and $b = -65$ calories/mol $\times$ K.

We have plotted all the points for the yeasts, virus and bacteria in Fig. 2. In Table 1 we collect all the values of the constants for comparison. The unicellular organisms have a specific death rate for thermal killing which follows a compensation law with constants which are in very good agreement with the constants for thermal denaturation of proteins. We suggest that this is good quantitative support for the general hypothesis that protein denaturation is the cause of thermal death in unicellular organisms. Such a statement, however, does not allow the identification of any specific protein as the limiting cause, because the cells will have different $\Delta S^\ddagger$, $\Delta H^\ddagger$ values in different environmental conditions, and any specific protein will exhibit a class of $\Delta S^\ddagger$, $\Delta H^\ddagger$ values in different environmental conditions *in vitro*. It may be possible, though difficult, to find an isolatable protein, or group of proteins, the $\Delta S^\ddagger$, $\Delta H^\ddagger$ values of which *in vitro* coincide with those of

Table 1 Comparison of Compensation Law Constants, T_c and b , from: $\Delta S^\ddagger = a \Delta H^\ddagger + b$; $T_c = 1/a$

	T_c (K)	b (calories/mol $\times$ K)
Proteins	329	-64.9
Virus	330	-64
Yeasts	325	-64.5
Bacteria	331	-65

the cell for the same conditions, and draw the inference that this (these) is (are) the limiting protein(s). The viruses, constituted with a small number of proteins, recommend themselves for such a study.

In a cell, a protein i is manufactured with a creation rate c_i , and has a denaturation rate, $k_{D_i}n_i$ (again we ignore renaturation, although it could be subsumed under c_i); therefore we have:

$$\frac{dn_i}{dt} = c_i - k_{D_i}n_i \quad (3)$$

If a steady state could occur, then the number of molecules of protein i is $n_i = c_i/k_{D_i}$. The creation rate c_i must be assumed to be a complex function of both the genetic structure and environmental conditions. For a population of cells to die with pseudo-first order kinetics, the temperature must be high enough that the denaturation rate overwhelms the ability of the cell to create the proteins that are limiting, and $dn_i/dt = k_{D_i}n_i$. If N is the number of viable cells, then our hypothesis requires that $dN/dt = -k_{D_i}N$. It is not obvious why the k_{D_i} for the cell population should be identical with k_{D_i} for the protein population. For example, the assumption that a threshold number of proteins, i , is essential for cell viability would lead to a single time instant of death for all the cells of the population, rather than a constant probability of death as the kinetics require. It can be shown mathematically that at least three hypotheses connecting protein denaturation with cell death could lead to the appropriate kinetics and thermodynamics. These are (a) that there is a statistical distribution of protein concentration thresholds in the population of cells; (b) that the stress on the cell to create protein at a rate sufficient to compensate the denaturation rate is the cause of death; and (c) that the stress on the cell to prevent the accumulation of denatured protein

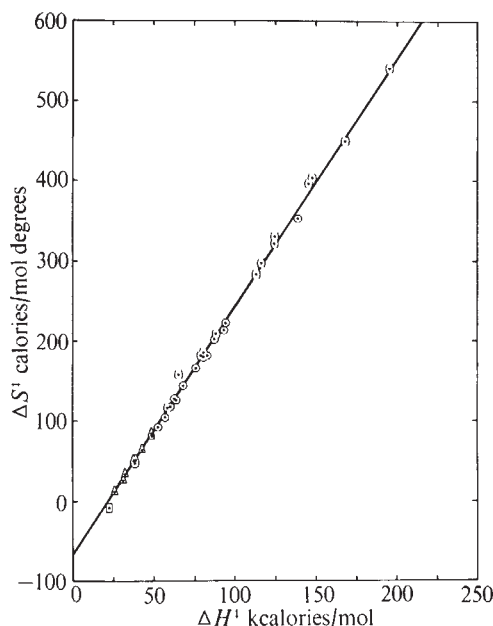


Fig. 2 A plot of the activation entropy, $\Delta S^\ddagger$, versus the activation enthalpy, $\Delta H^\ddagger$, for thermal killing of various organisms: $\circ$, yeasts (after van Uden *et al.*¹³); $\square$, bacteria (after Lueddecke¹⁵, Walker¹⁶, and Beamer and Tanner¹⁷); $\triangle$, virus (after Barnes *et al.*¹⁴); and $\diamond$, *Drosophila m.* (after Strehler¹⁸). The constants of the line are: $T_c = 325$ K and $b = -66$ calories/mol $\times$ K.

debris kills the cell. There are undoubtedly other possible hypotheses which should be tested.

In Fig. 2 we have plotted a single point on the line which refers to the multicellular poikilotherm, *Drosophila melanogaster*, after the data of Strehler¹⁸. We have replotted his death rate curves to obtain the first order kinetic plots versus time. These k_D s do show an exponential dependence on the temperature; and using equation (1), we have calculated the $\Delta S^\ddagger$ for these data. The datum point falls on the line close to the $\Delta S^\ddagger \approx 0$ value. Strehler¹ has pointed out that a number of other studies on arthropods (*Drosophila*, *Pinus tectus* and *Daphnia*) have shown almost identical activation energies for the rate of ageing (as measured by the mortality rate) and these would yield data points close to $\Delta S^\ddagger \approx 0$, according to our estimates. We can now speculate that, if this is so, it has at least two explanations. First, the evolutionary jump from unicellular to multicellular organisms can be represented on the compensation law plot as the convergence of the $\Delta H^\ddagger$ values to the lowest value consonant with $\Delta S^\ddagger \geq 0$. That means that the arthropods have accepted a higher thermal death rate still consistent with survival of the species, for a smaller variation of the thermal denaturation rate of the limiting proteins with ambient temperature changes. Second, Sukhorukov and Likhtenshtein¹² have shown that many dry proteins fall on the compensation law plot at $\Delta S^\ddagger \approx 0$, and that hydration of these proteins causes the $\Delta S^\ddagger$, $\Delta H^\ddagger$ values to move up the line. $\Delta S^\ddagger \approx 0$ may be the smallest value that can be reasonably expected in biological circumstances; therefore one could argue that in going up the evolutionary scale, "dry" proteins are first encountered in vital roles at the level of multicellular organisms. Because these proteins denature fastest, they represent the rate limiting step in the death of these organisms. These latter arguments are purely speculative.

This work was supported in part by contracts from the Office of Naval Research and the Atomic Energy Commission.

Note added in proof. A fourth hypothesis connecting protein denaturation and cell death was proposed by Rahn in 1929 (Rahn, O., *Bact. Rev.*, **8**, 1; 1944). According to him, "a logarithmic order is possible only when death is due to the destruction of a single protein molecule in the cell". We find this the most attractive alternative, with some interesting ramifications which we will develop later.

BARNETT ROSENBERG
GABOR KEMENY
ROBERT C. SWITZER
THOMAS C. HAMILTON

Department of Biophysics, Michigan State University,
East Lansing, Michigan 48823

Received February 8, 1971.

- ¹ Strehler, B. L., *Time, Cells and Aging* (Academic Press, New York, 1962).
- ² Glasstone, S., Laidler, K. J., and Eyring, H., *The Theory of Rate Processes* (McGraw-Hill, New York, 1941).
- ³ Williams, T. P., and Milby, S. E., *Vision Res.*, **8**, 359 (1968).
- ⁴ Rosenberg, B., and Williams, T. P., *Vision Res.* (in the press).
- ⁵ Eley, D. D., *J. Polymer Sci.*, Pt C, **17**, 73 (1967).
- ⁶ Rosenberg, B., Bhowmik, B. B., Harder, H. C., and Postow, E., *J. Chem. Phys.*, **49**, 4108 (1968).
- ⁷ Lumry, R., and Rajender, S., *Biopolymers*, **9**, 1125 (1970).
- ⁸ McCreary, J. R., and Thorn, R. J., *J. Chem. Phys.*, **50**, 3725 (1969).
- ⁹ Leffler, J., and Grunwald, E., *Rates and Equilibria of Organic Reactions* (Wiley, New York, 1963).
- ¹⁰ Exner, O., *Nature*, **201**, 488 (1964).
- ¹¹ Joly, M., *A Physico-Chemical Approach to Denaturation of Proteins* (Academic Press, New York, 1965).
- ¹² Sukhorukov, B. I., and Likhtenshtein, G. I., *Biofizika*, **10**, 935 (1965).
- ¹³ van Uden, N., Abranches, P., and Cabeca-Silva, C., *Archiv. Mikrobiol.*, **61**, 381 (1968).
- ¹⁴ Barnes, R., Vogel, H., and Gordon, I., *Proc. US Nat. Acad. Sci.*, **62**, 263 (1969).
- ¹⁵ Lueddecke, L. O., thesis, Michigan State Univ. (1962).
- ¹⁶ Walker, G. C., thesis, Michigan State Univ. (1964).
- ¹⁷ Beamer, P. R., and Tanner, F. W., *Zentralblatt Bakt.*, **100**, 81 (1939).
- ¹⁸ Strehler, B. L., *J. Gerontol.*, **16**, 2 (1961).

Preparation and Characterization of an Arylsulphatase insolubilized on Porous Glass

THE enzyme sterol sulphate sulphohydrolase (EC 3162) is used for the hydrolysis of steroid conjugates before analysis of body fluids for total oestrogens; but it is rather costly. The availability of a re-usable derivative of this enzyme which would be stable for a long time might be of value to the clinical chemist. I therefore decided to prepare an insolubilized derivative of this enzyme and determine its properties.

The enzyme was purchased as a mixture of β -glucuronidase/arylsulphatase (Boehringer). The arylsulphatase activity of the commercial preparation was 2.6 IU/ml. of enzyme solution. The insoluble enzyme was prepared as previously described¹⁻³. Porous glass used for this study was 96% silica particles, pore diameter 550 Å, 40/60 mesh particle size. The enzyme was coupled through azo linkage to the glass. The insoluble enzyme was assayed with 0.001 M *p*-nitrophenylsulphate dissolved in 0.25 M Na₂CO₃ buffer (pH 9.0). The assay was carried out using 25 ml. of substrate to which was added a known weight of enzyme derivative. The reaction was continued for 10 min after which a sample was taken and read spectrophotometrically at 410 nm. The reaction was carried out at 25° C. Activity of the final product was 0.31 IU/g of glass. All other studies were carried out by the column method.

One gram of derivative was packed into a small, glass, 1.0 cm wide, jacketed column to a height of 5.0 cm. Temperature was maintained at 6° C throughout these studies.

A pH profile was obtained by passing 1×10^{-5} M *p*-nitrophenylsulphate through the column at a flow rate of 0.67 ml./min. The column effluent was continuously monitored at 410 nm in a flowthrough colorimeter. The buffers used were 0.25 M acetate between pH 5.0 and 6.7 and carbonate between pH 7.8 and 10.5. The pH optimum lies between pH 9.0 and 9.5 (Fig. 1).

By passing substrate at increasing concentrations through the column while maintaining constant flow rate (0.67 ml./min), the values for K_m and V_{max} were obtained (Fig. 2). The apparent V_{max} for the insoluble enzyme was 1.67×10^{-8} mol/s. The apparent K_m was 1.57×10^{-3} M. These values were

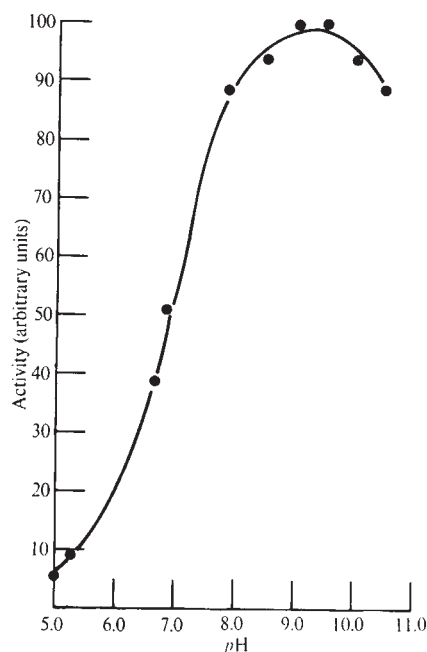


Fig. 1 pH profile using 1×10^{-5} M *p*-nitrophenylsulphate as substrate.

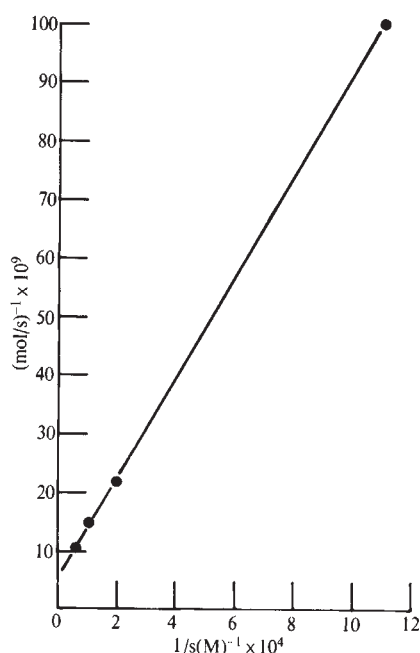


Fig. 2 Plot of $1/v$ against $1/(S)$. Substrate was *p*-nitrophenylsulphate in 0.25 M NaCO_3 (pH 9.0).

within 20% of values we obtained experimentally for the soluble enzyme at the same enzyme concentration.

The hydrolytic rate using 2.5×10^{-4} M substrate was found, as expected, to be inversely related to flow rate (Fig. 3). The relationship is not inversely proportional, however, and the curve seems very quickly to become asymptotic. Although the difference in flow rate between 0.67 ml./min and 3.0 ml./min is approximately 4.5 $\times$, the product concentration is decreased only 70%. The actual enzyme velocity of the insoluble derivative thus seems to increase with increasing flow rate, causing the asymptotic curvature. The apparent increased velocity is probably caused by the increased turbulent flow which decreases the film layer resistance at the surface of the particles. Because the substrate concentration used for the experiment was less than K_m , the decreased film resistance allowed more rapid diffusion of substrate. The enzyme, seeing substrate concen-

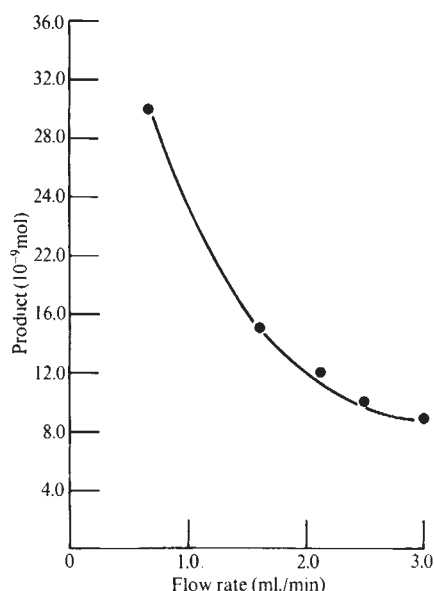


Fig. 3 Flow rate against product formation. Substrate was 2.5×10^{-4} M *p*-nitrophenylsulphate in 0.25 M NaCO_3 (pH 9.0).

trations below that necessary to maintain $V_{\max}$, produced more product when exposed to higher substrate concentrations.

The same insoluble enzyme preparation was used for all the above described experiments. The entire study took 4 weeks. At the end of this time the derivative was removed from the column and assayed. No losses of activity had occurred.

This study has shown that an arylsulphatase can be insolubilized. The insolubilized enzyme is active, stable and can be re-used many times within at least 30 days.

H. H. WEETALL

Research and Development Laboratories,
Corning Glass Works,
Corning,
New York 14830

Received March 12, 1971.

¹ Weetall, H. H., *Nature*, **223**, 959 (1969).

² Weetall, H. H., *Science*, **166**, 615 (1969).

³ Weetall, H. H., *Biochim. Biophys. Acta*, **212**, 1 (1970).

Possible Role of Cyclic AMP in the Short Term Regulation of Adrenal Steroidogenesis

THE most significant short term physiological effect of adrenocorticotrophic hormone (ACTH) is to increase the rate of adrenal steroid hormone synthesis and secretion^{1,2}. There is a great deal of evidence for adenosine 3',5'-monophosphate (cyclic AMP) as intracellular mediator of this acute steroidogenic response³⁻⁹. The following steps are probably involved²: ACTH increases adrenocortical adenyl cyclase activity, thus raising the intracellular concentration of cyclic AMP which in turn enhances the conversion of cholesterol to pregnenolone, normally the rate-limiting reaction. Much of the evidence for this concept comes from experiments on intact cells though the enhancement of a variety of steroid hydroxylations in cell-free adrenal preparations by cyclic AMP has been reported¹⁰⁻¹³.

Recently Koritz *et al.*¹⁴ found that cyclic AMP and several chemically related compounds inhibited the conversion of cholesterol to progesterone in beef adrenocortical mitochondria; and that, in rat adrenal homogenates, cyclic AMP diminished overall corticosteroid formation by inhibiting the conversion of pregnenolone to progesterone. These observations have been confirmed by others (ref. 15 and unpublished results of J. D. Jones and myself). The conversion of Δ^5 - β -hydroxysteroids to their Δ^4 -3-ketosteroid products is essential in the formation of the active steroid hormones. It is catalysed by the consecutive action of a β -hydroxysteroid dehydrogenase (β -HSD) and 3-ketosteroid isomerase (3-KSI) present in both the microsomal and mitochondrial subcellular fractions^{15,16}. NAD^+ is the preferred cofactor for the dehydrogenase¹⁷ while both NAD^+ and NADH are potent activators of the 3-KSI¹⁸. Cyclic AMP and chemically related compounds inhibit the NAD^+ and NADH -dependent activation of beef adrenocortical 3-KSI^{16,18} and inhibit β -HSD activity competitively with respect to the cofactor NAD^+ ^{15,16}. Cyclic AMP is the most potent inhibitor; the suppression of corticosterone synthesis in crude adrenal homogenates is observed with concentrations of cyclic AMP above 0.2 mM and the K_i for cyclic AMP inhibition of the microsomal 3-HSD activity has been estimated to range (according to my unpublished results) from 19 to 270 μM and from 121 to 192 μM ¹⁶. In the absence or in the presence of varying concentrations of cyclic AMP β -HSD activity is rate-limiting in the conversion of Δ^5 - β -hydroxysteroids to their Δ^4 -3-ketosteroid products¹⁶.

These data from cell-free preparations may reflect an unsuspected inhibitory role for cyclic AMP in a relatively intact system. The experiments of Grahame-Smith *et al.*⁶ on intact

rats are compatible with this contention: administration of large amounts of ACTH (≥ 50 mU) to rats caused an increase of the adrenal cyclic AMP to a maximum of 0.45 mmol/kg tissue. But the injection of only 2 mU of ACTH, resulting in a cyclic AMP concentration of about 25 μ mol/kg adrenal tissue, proved maximally stimulatory for corticosteroidogenesis. This suggests that with larger doses of ACTH the rising adrenal level of cyclic AMP prevented a continued increase in the rate of corticosterone formation.

The following hypothesis is an attempt to reconcile the concept of cyclic AMP as intracellular mediator of the acute steroidogenic response to ACTH with its inhibitory action described here.

I propose that a small increase in plasma ACTH results in a correspondingly small increase in the intra-adrenal concentration of cyclic AMP, sufficient to enhance the conversion of cholesterol to pregnenolone and promote steroidogenesis. The ratio of C21 to C19 steroid hormone formation will depend on intracellular compartmentation and on the kinetic parameters and activities of the enzymes involved in the two pathways. With further increase in plasma ACTH the adrenal cyclic AMP level rises sufficiently to cause significant inhibition of the conversion of Δ^5 -3 β -hydroxysteroids to Δ^4 -3-ketosteroids by competing with NAD⁺ for binding to the 3 β -HSD. Fig. 1 shows that in these conditions steroidogenesis is specifically directed towards dehydroepiandrosterone (DHEA) rather than corticosteroid and androgen formation. Thus ACTH, depending on its plasma level, may invoke at least two patterns of adrenal steroid hormone synthesis for both of which cyclic AMP is the intracellular mediator. These may overlap considerably with a gradually increasing emphasis on DHEA secretion with respect to the Δ^4 -3-ketosteroids. Finally, high adrenal cyclic AMP concentrations may, by raising the intracellular level of pregnenolone, inhibit the side-chain cleavage of cholesterol and hence overall steroidogenesis.

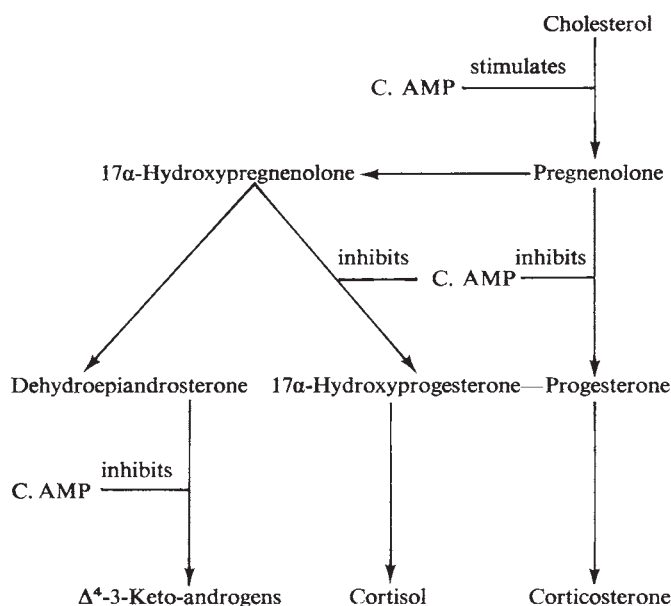


Fig. 1

The following points are relevant to a consideration of my thesis. ACTH exerts a variety of long term effects on adrenocortical function including the enhancement of specific enzyme activities^{20,21} and the overall promotion of adrenal growth²². While these actions undoubtedly bear on the steroidogenic response to prolonged ACTH stimulation, they are not material to my hypothesis which is concerned with the acute regulation of steroid biogenesis. The validity of the hypothesis is independent of the mechanism whereby cyclic AMP stimulates the conversion of cholesterol to pregnenolone; nor is it necessarily

affected by evidence²³ that 17 α -hydroxypregesterone rather than progesterone is the quantitatively more significant intermediate of cortisol biosynthesis. The validity of the hypothesis largely rests on whether, in physiological conditions, cyclic AMP reaches concentrations capable of effectively competing with available NAD⁺ for binding to adrenal 3 β -HSD. This may depend on some degree of intracellular compartmentation of cyclic AMP (ref. 16, and unpublished results of J. D. Jones and myself). Regulation of adrenal steroidogenesis by cyclic AMP is probably modified by the capacity of some C19 steroid intermediates to inhibit 3 β -HSD activity¹⁹, by the participation of steroid sulphates in biosynthesis and by the intracellular compartmentation of substrates, cofactors, and enzymes.

The hypothesis is compatible with some data derived from more physiological systems. The intravenous administration of large doses of ACTH to human subjects elicits a rapid and marked increase in adrenal DHEA secretion²⁴. Urquhart *et al.*²⁵, in a study of the mechanisms underlying the regulation of corticosteroidogenesis, included a saturable enzyme step subsequent to cholesterol side-chain cleavage. According to my hypothesis stimulation by ACTH could cause the adrenal concentration of pregnenolone and 17 α -hydroxypregnenolone to rise to levels at which zero order kinetics would hold for their conversion into their respective Δ^4 -3-keto products.

The biological significance of the hypothesis remains to be determined. In species such as rodents, lacking significant 17-hydroxylase activity, adrenal dehydroepiandrosterone secretion would be negligible regardless of adrenal cyclic AMP levels. In other species, including man, DHEA (sulphate) secretion may be considerable at high plasma ACTH and adrenal cyclic AMP concentrations. As well as possessing insignificant intrinsic androgenic activity DHEA seems to be a limited peripheral precursor of the more potent sex hormones²⁶, except in the placenta²⁷. Thus the diversion of steroid biosynthesis towards DHEA production may be a means of avoiding excessive and inappropriate androgen, and possibly corticosteroid, secretion in response to ACTH. Yang and Deal²⁸ have reported that cyclic AMP and related compounds inhibit yeast glyceraldehyde 3-phosphate dehydrogenase by a mechanism analogous to cyclic AMP inhibition of 3 β -HSD. The direct inhibition of key dehydrogenases by cyclic AMP may have hitherto unsuspected significance in metabolic regulation.

G. M. B. BERGER

Red Cross War Memorial
Children's Hospital,
Rondebosch,
Cape,
South Africa

Received June 17; revised September 19, 1970.

- Robison, G. A., Butcher, R. W., and Sutherland, E. W., *Ann. Rev. Biochem.*, **37**, 149 (1968).
- Catt, K. J., *Lancet*, **i**, 1279 (1970).
- Haynes, jun., R. C., *J. Biol. Chem.*, **233**, 1220 (1958).
- Haynes, jun., R. C., Koritz, S. B., and Peron, F. G., *J. Biol. Chem.*, **234**, 1421 (1959).
- Karaboyas, G. C., and Koritz, S. B., *Biochemistry*, **4**, 462 (1965).
- Grahame-Smith, D. G., Butcher, R. W., Ney, R. L., and Sutherland, E. W., *J. Biol. Chem.*, **242**, 5535 (1967).
- Taunton, O. D., Roth, J., and Pastan, I., *Biochem. Biophys. Res. Commun.*, **29**, 1 (1967).
- Hilton, J. G., Kruesi, O. R., Nedeljkovic, R. I., and Scain, L. F., *Endocrinology*, **68**, 908 (1961).
- Imura, H., Matsukura, S., Matsuyama, H., Setsuda, T., and Miyaka, T., *Endocrinology*, **76**, 933 (1965).
- Roberts, S., Creange, J. E., and Fowler, D. D., *Nature*, **203**, 759 (1964).
- Creange, J. E., and Roberts, S., *Biochem. Biophys. Res. Commun.*, **19**, 73 (1964).
- Roberts, S., Creange, J. E., and Young, P. L., *Biochem. Biophys. Res. Commun.*, **20**, 446 (1965).
- Roberts, S., McCune, W. R., Creange, J. E., and Young, P. L., *Science*, **158**, 372 (1967).
- Koritz, S. B., Yun, J., and Ferguson, jun., J. J., *Endocrinology*, **82**, 620 (1968).

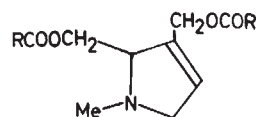
- ¹⁵ Sulimovici, S., and Boyd, G. S., *Europ. J. Biochem.*, **7**, 549 (1969).
- ¹⁶ McCune, R. W., Roberts, S., and Young, P. L., *J. Biol. Chem.*, **245**, 3859 (1970).
- ¹⁷ Koritz, S. B., *Biochemistry*, **3**, 1098 (1964).
- ¹⁸ Oleinick, N. L., and Koritz, S. B., *Biochemistry*, **5**, 715 (1966).
- ¹⁹ Kowal, J., Forchielli, E., and Dorfman, R. I., *Steroids*, **4**, 77 (1964).
- ²⁰ Kowal, J., *Biochemistry*, **8**, 1821 (1969).
- ²¹ Kowal, J., Simpson, E. R., and Estabrook, R. W., *J. Biol. Chem.*, **245**, 2438 (1970).
- ²² Bransome, jun., E. D., *Ann. Rev. Physiol.*, **30**, 171 (1968).
- ²³ Deshpandu, N., Jensen, V., and Doooss, I. W., *J. Endocrinol.*, **43**, XIV (1969).
- ²⁴ Vaitukaitis, J. L., Dale, S. I., and Melby, J. C., *J. Clin. Endocrinol.*, **29**, 1443 (1969).
- ²⁵ Urquhart, J., Krall, R. L., and Li, C. C., *Endocrinology*, **83**, 390 (1968).
- ²⁶ Baird, D. T., Horton, R., Longcope, C., and Tait, J. F., *Rec. Prog. Hormone Res.*, **25**, 611 (1969).
- ²⁷ Vilee, D. B., *New Engl. J. Med.*, **218**, 473 (1969).
- ²⁸ Yang, S. T., and Deal, jun., W. C., *Biochemistry*, **8**, 2806 (1969).

Synthetic Compounds with Toxic Properties similar to those of Pyrrolizidine Alkaloids and their Pyrrolic Metabolites

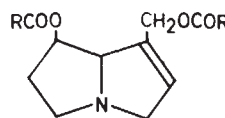
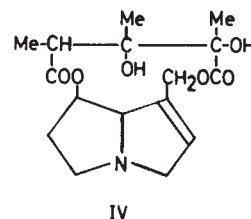
FOR the first time, some of the toxic effects of unsaturated pyrrolizidine alkaloids on rats have been reproduced by dosing animals with synthetic compounds. Many of the naturally occurring hepatotoxic alkaloids are esters of the isomeric amino-alcohols retronecine or heliotridine with various branched chain hydroxy-acids¹. The most toxic alkaloids are cyclic diesters of retronecine¹, which are particularly resistant to enzymic hydrolysis. Because hepatotoxicity of the pyrrolizidine alkaloids has been associated with the metabolic conversion of the pyrroline to a pyrrole ring^{2,3}, with retention of the ester groups⁴, it was expected that simpler pyrroline esters would have similar toxic properties provided that the ester groups were resistant to enzymic hydrolysis.

Of the compounds I have prepared and tested, the most effective are carbamate esters of 1-methyl-2,3-bis-hydroxy-methyl-3-pyrroline. The N-ethyl carbamate diester (I) of this amino-alcohol is rather more toxic than the natural alkaloid monocrotaline (IV). In preliminary experiments, pyrrolic metabolites were demonstrated⁵ in the livers, lungs and urine of male rats 2 h after intraperitoneal injection of this synthetic compound. Most animals given doses of more than 60 mg/kg body weight died 2–6 days later and had bloodstained ascites and massive haemorrhagic centrilobular liver necrosis. Histologically, this was characteristic of the type of damage caused by pyrrolizidine alkaloid poisoning⁶. Similar effects were seen after oral administration of the compound. Rats surviving for 3 weeks had the characteristic giant liver cells (megacytes)⁷ and these were abundant in livers of rats which had been given the compound intraperitoneally (30–40 mg/kg) at the age of 4 days. After very large doses (160–250 mg/kg) the animals usually died on the second or third day with their chests full of pale yellow fluid. It has been suggested^{8,9} that lung damage due to pyrrolizidine alkaloids may be caused by some of the metabolite formed in the liver escaping to the lungs.

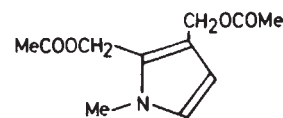
The analogous diacetyl and di-isovaleryl esters (II and III) were not toxic to rats at much larger doses than the carbamate, and were not metabolized to significant amounts of pyrrole derivatives. The choice of carbamate esters was made from previous experience with semisynthetic retronecine diesters. Hepatotoxicity has been demonstrated¹⁰ in esters such as di-isovaleryl retronecine (V)¹¹ when doses larger than 250 mg/kg were administered to rats, but diacetyl retronecine (VI) was hepatotoxic only in much larger doses and after the animals had been treated with an esterase inhibitor⁹. It was thought that rapid hydrolysis by esterases to the highly water



- I R = EtNH
 II R = Me
 III R = Me₂CHCH₂



- V R = Me₂CHCH₂
 VI R = Me
 VII R = EtNH



soluble amino-alcohol might be responsible for the low toxicities of semisynthetic esters and that carbamates might be more resistant to such hydrolysis, or even inhibitory to esterases¹². The semisynthetic N-ethyl carbamate diester of retronecine (VII) was therefore prepared, and its toxicity to the rat was similar to that of monocrotaline (IV)¹³. The synthetic carbamate (I) subsequently proved to be even more toxic.

Characteristic toxic effects in the lungs of rats have been found after intravenous injection of pyrrolic esters derived from natural pyrrolizidine alkaloids, such as monocrotaline pyrrole¹⁴, and semisynthetic esters such as diacetyl retronecine pyrrole⁹. We have now obtained the same effects using the entirely synthetic compound, 1-methyl-2,3-diacetoxymethyl pyrrole (VIII). Injections of 5–12 mg/kg of this compound into the tail veins of rats of either sex often caused death after 20–35 days and produced changes in the lungs similar to those described earlier for monocrotaline pyrrole¹⁴. Some centrilobular liver necrosis was also seen. Larger doses caused massive pleural effusions and death within a few days.

The results described here are consistent with the view that chemically reactive pyrrolic metabolites are responsible for cytotoxic effects of pyrrolizidine alkaloids, and show for the first time that such effects can be caused by compounds with a single five membered ring. It follows that studies of the types of experimental liver and lung lesions described here need no longer depend on supplies of natural pyrrolizidine alkaloids. Chemically modified and radioactive labelled compounds will be more readily available for investigations of mechanisms of toxic action. Tumour-inhibitory activity has been observed with some of the natural alkaloids¹⁵ and their pyrrolic derivatives³, and the use of synthetic analogues might enable this property to be exploited more effectively. Further studies of the toxic and other effects of these and related synthetic compounds are in hand and will be reported in detail elsewhere.

I thank Drs J. M. Barnes and W. H. Butler for help with the pathology and R. Jones for technical assistance.

A. R. MATTOCKS

Toxicology Unit,
 MRC Laboratories,
 Woodmansterne Road,
 Carshalton, Surrey

Received March 11; revised April 30, 1971.

¹ Schoental, R., *Israel. J. Med. Sci.*, **4**, 1133 (1968).

² Mattocks, A. R., *Nature*, **217**, 723 (1968).

³ Culvenor, C. C. J., Downing, D. T., Edgar, J. A., and Jago, M. V., *Ann. NY Acad. Sci.*, **163**, 837 (1969).

⁴ Mattocks, A. R., and White, I. N. H., *Nature New Biology*, **231**, 114 (1971).

⁵ Mattocks, A. R., and White, I. N. H., *Anal. Biochem.*, **38**, 529 (1970).

⁶ Davidson, J., *J. Path. Bact.*, **40**, 285 (1935).

⁷ Schoental, R., and Magee, P. N., *J. Path. Bact.*, **74**, 305 (1957).

- ⁸ Barnes, J. M., Magee, P. N., and Schoental, R., *J. Path. Bact.*, **88**, 521 (1964).
⁹ Mattocks, A. R., *Nature*, **228**, 174 (1970).
¹⁰ Schoental, R., and Mattocks, A. R., *Nature*, **185**, 842 (1960).
¹¹ Mattocks, A. R., *J. Chem. Soc. (C)*, 2698 (1969).
¹² Baron, R. L., Casterline, J. L., and Orzel, R., *Toxicol. Appl. Pharmacol.*, **9**, 6 (1966).
¹³ Schoental, R., and Magee, P. N., *J. Path. Bact.*, **78**, 471 (1959).
¹⁴ Butler, W. H., Mattocks, A. R., and Barnes, J. M., *J. Path.*, **100**, 169 (1970).
¹⁵ McLean, E. K., *Pharmacol. Rev.*, **22**, 429 (1970).

Tolerance to Opioid Narcotics: Time Course and Reversibility of Physical Dependence in Mice

REPEATED administration of an opiate narcotic leads to the tolerant-dependent state. Previous communications^{1,2} from this laboratory have described the relationship between the degree of tolerance in mice and the dose, interval and duration of exposure to an opiate. Recently, jumping behaviour elicited by the opiate antagonist, naloxone, was shown to be a sensitive indicator of the degree of dependence³. We have used this method to follow the time courses of the onset and reversal of dependence in various conditions of exposure to opiates.

Male Swiss-Webster mice weighing 25–30 g were used. Water and Purina laboratory food were freely available. Levorphanol tartrate, a synthetic congener of morphine, was supplied by Hoffmann-LaRoche Inc. Naloxone hydrochloride was a gift of Endo Laboratories and morphine alkaloid was purchased from Mallinckrodt Chemicals Inc. Doses are expressed in terms of the free bases. All injections were intraperitoneal.

Physical dependence on morphine was produced by implanting a specially formulated 75 mg morphine pellet⁴, without anaesthesia, in the subcutaneous tissue of the back. Animals so implanted display analgesia and vigorous running activity for less than 24 h. Release of morphine from the pellet proceeds linearly for longer than the time of our experiments⁵.

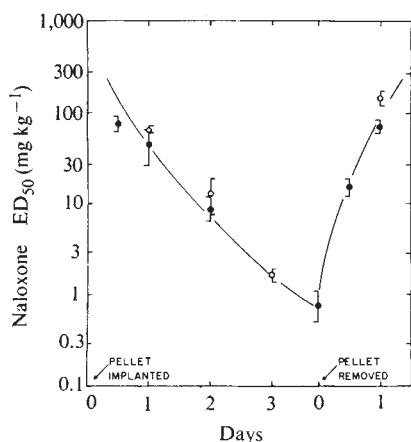


Fig. 1 Development and reversibility of physical dependence. The ED₅₀ for naloxone-induced jumping is plotted on a logarithmic scale against time. Mice were implanted with 75 mg morphine pellets. Groups were tested with naloxone at various times, then discarded; pellets remained in place during testing. After 3.7 days pellets were removed from all remaining animals in order to follow the recovery process and 2 days later groups of mice were re-implanted on the opposite side with fresh pellets, which were also removed after 3.7 days. Solid circles represent the first cycle of dependence and recovery, open circles represent the second cycle. Standard errors of the ED₅₀ estimates are shown by brackets above and below each data point. In these experiments 325 mice were implanted initially; each point is based on twenty-four to thirty-three animals.

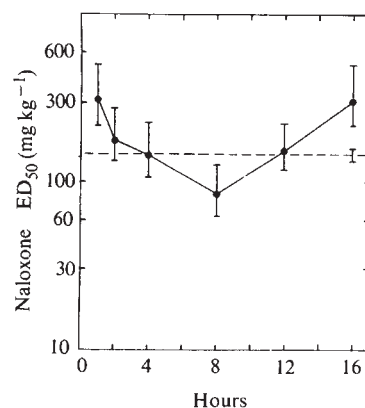


Fig. 2 Initiation of physical dependence by a single dose of levorphanol. At time zero, mice were given a single intraperitoneal 20 mg kg⁻¹ levorphanol injection. Groups were tested with several doses of naloxone at various times thereafter to determine the ED₅₀ for precipitated jumping. The dashed line indicates the ED₅₀ for naloxone-induced convulsions in control mice. Each ED₅₀ above the dashed line is an extrapolation from the lower dose segment of a quantal log dose-response curve obtained at the given time. Standard errors of the ED₅₀ estimates are shown by brackets above and below each data point. Each point is based on forty-five animals.

Naloxone was used to precipitate withdrawal jumping, as described by Maggiolo and Huidobro⁵ and Way *et al.*³. The ED₅₀ (median effective dose) of naloxone was determined according to Litchfield and Wilcoxon⁶ or by the more economical "up and down" method of Dixon⁷, in which five mice were injected and placed on the platform together. If a mouse jumped off within 10 min, the dose for its replacement was halved; otherwise, the dose for its replacement was doubled. Thus, five replicate series were obtained. Groups of mice were tested at different times, but each group was tested once only, then discarded.

In untreated mice, no dose of naloxone would induce jumping, but in opiate-dependent mice, doses of about 150 mg kg⁻¹ or less were effective: the smaller the degree of dependence, the higher the necessary dose of naloxone. The method was limited by the fact that naloxone itself, in dependent as well as untreated mice, causes convulsions at high doses (ED₅₀ = 150 ± 13 mg kg⁻¹ in untreated mice) so that a very small degree of dependence could not be measured.

After implantation of a morphine pellet, the sensitivity to naloxone became progressively greater for more than 3 days (Fig. 1). The time course of the approach to a steady state is evidently measured in days, although in these experiments a constant level of dependence was not quite reached. The process was completely reversible after removal of the pellet, and the return to normal was complete in 24 h. A group of the same animals was re-implanted and the entire cycle of onset and disappearance of dependence observed. The high degree of dependence produced in the first cycle clearly had no modifying effect on the second cycle, which was, within the limits of experimental error, identical to the first. The disappearance of dependence so much faster than it develops has interesting theoretical implications^{8–10}.

A single moderate dose of levorphanol (20 mg kg⁻¹) produced a definite but small degree of dependence (Fig. 2). (The ED₅₀ of levorphanol for running activity and analgesia is 2.3 mg kg⁻¹; see ref. 1.) The process is evidently initiated immediately, reaches its peak after about 8 h, then wanes and disappears after 16 h. Naloxone can elicit jumping 16 h after a single injection although levorphanol has a very short half-life—less than 1 h—in plasma and brain of the mouse (unpublished observations of A. G.). As might be expected, injection of the same dose of levorphanol every 12 h produced only a small degree of dependence at the steady state, whereas injection every 4 h produced an increasing degree of dependence (Fig. 3).

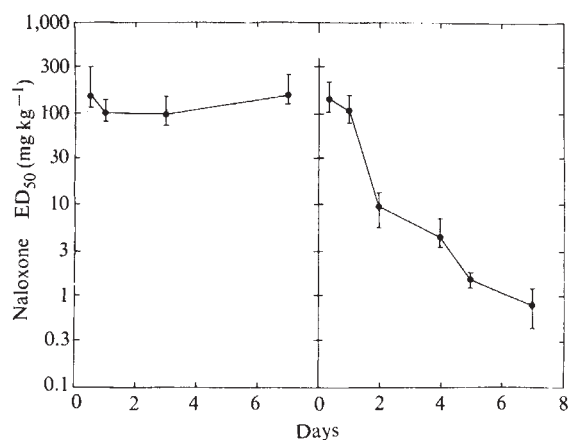


Fig. 3 Development of physical dependence on 12 h (left) and 4 h (right) schedules of levorphanol injections (20 mg kg^{-1}). Groups were tested with several concentrations of naloxone 12 h or 4 h, respectively, after the previous injection of levorphanol to determine the ED_{50} values for naloxone-induced jumping. Symbols are as in Fig. 2.

We have shown here that in the mouse, a single dose of opiate produces a certain quantum of physical dependence, which dissipates entirely in about 24 h. A small degree of dependence can also be produced by a single dose of opiate in the spinal dog¹¹. In our experiments, frequent injections of levorphanol or implantation of a morphine pellet caused a cumulative build up of dependence. Injections at a long enough interval caused no build up of dependence, regardless of the duration of administration of the drug. These findings agree with our observations on tolerance^{1,2}: the frequency of administration of a fixed dose controls the level of the steady state attained. Anecdotal evidence suggests a similar phenomenon in human narcotic addiction; tolerance and dependence probably do not develop at dose frequencies lower than about 0.5–1.0/day^{12,13}.

We have also shown that physical dependence in the mouse, like tolerance, is completely and rapidly reversible, and that one cycle of dependence and recovery does not modify the course of a subsequent cycle. On the other hand, Wikler and Pescor¹⁴ demonstrated long lasting residual effects of an addiction cycle in rats. Goldberg and Schuster¹⁵ showed, in monkeys, that naloxone could precipitate certain physiological disturbances months after morphine withdrawal, and in man Martin and co-workers^{16,17} found that abnormalities similar to those of the withdrawal syndrome persisted for months after the principal withdrawal effects had terminated. We are not able to explain the differences between these results and our own.

This investigation was supported by a research grant from the National Institute of Mental Health and by a training grant from the National Institute of General Medical Sciences. We thank Dr R. D. Gibson for morphine pellets. (Some of the findings reported here were the subject of a preliminary communication¹⁸.)

D. L. CHENEY
AVRAM GOLDSTEIN

Department of Pharmacology,
Stanford University School of Medicine,
Stanford, California

Received December 23, 1970; revised March 16, 1971.

- ¹ Goldstein, A., and Sheehan, P., *J. Pharmacol. Exp. Ther.*, **169**, 175 (1969).
- ² Richter, J. A., and Goldstein, A., *Proc. US Nat. Acad. Sci.*, **66**, 944 (1970).
- ³ Way, E. L., Loh, H. H., and Shen, F., *J. Pharmacol. Exp. Ther.*, **167**, 1 (1969).
- ⁴ Gibson, R. D., and Tingstad, J. E., *J. Pharmac. Sci.*, **59**, 426 (1970).

- ⁵ Maggiolo, C., and Huidobro, F., *Acta Physiol. Latin Amer.*, **11**, 70 (1961).
- ⁶ Litchfield, jun., J. T., and Wilcoxon, F., *J. Pharmacol. Exp. Ther.*, **96**, 99 (1949).
- ⁷ Dixon, W. J., *J. Amer. Stat. Assoc.*, **60**, 967 (1965).
- ⁸ Goldstein, D. B., and Goldstein, A., *Biochem. Pharmacol.*, **8**, 48 (1961).
- ⁹ Goldstein, A., and Goldstein, D. B., *Assoc. Res. Nerv. Mental Dis. Res. Pub.*, **46**, 265 (1968).
- ¹⁰ Goldstein, A., Aronow, L., and Kalman, S. M., *Principles of Drug Action* (Harper and Row, New York, 1968).
- ¹¹ Wikler, A., and Carter, R. L., *J. Pharmacol. Exp. Ther.*, **109**, 92 (1953).
- ¹² Kolb, L., *Drug Addiction* (Thomas, Springfield, Illinois, 1962).
- ¹³ Chein, I., Gerard, D. L., Lee, R. S., and Rosenfeld, E., *The Road to H* (Basic Books, New York, 1964).
- ¹⁴ Wikler, A., and Pescor, F. T., *Psychopharmacologia*, **10**, 255 (1967).
- ¹⁵ Goldberg, S. R., and Schuster, C. R., *Science*, **166**, 1548 (1969).
- ¹⁶ Martin, W. R., Jasinski, D. R., Sapira, J. D., Flanary, H. G., Kelly, O. A., Thompson, A. K., and Logan, C. R., *J. Pharmacol. Exp. Ther.*, **162**, 182 (1968).
- ¹⁷ Martin, W. R., and Jasinski, D. R., *J. Psychiat. Res.*, **7**, 9 (1969).
- ¹⁸ Cheney, D. L., Goldstein, A., and Sheehan, P., *Fed. Proc.*, **29**, 685 (1970).

Serological Demonstration of H-Y (Male) Antigen on Mouse Sperm

We have recently overcome certain technical difficulties in applying the cytotoxicity test to mouse spermatozoa and have been able to show directly that H-2 antigens are expressed on these cells¹, thus confirming less direct evidence leading to the same conclusion². We have since applied the cytotoxicity test to sperm with antisera directed against a number of other systems of mouse alloantigens, TL³, θ^4 , Ly-A⁵ and Ly-B⁵, but none of these has given a positive reaction with sperm. This is not surprising because these are all "differentiation antigens"⁶ expressed primarily on lymphoid cells. Another antigenic system which distinguishes one mouse from another is H-Y. The H-Y antigen is carried by male cells only and is responsible for the rejection of male tissues by females of the same inbred strain⁷.

In the case of H-Y, in contrast to the other antigenic systems referred to above, there has so far been no conclusive serological demonstration of the antigen *in vitro*. This obviously limits further analysis of the H-Y system and leaves much uncertainty as to the nature of the anti H-Y immune response in terms of humoral and cellular immune factors.

The following data establish three things: (a) H-Y antigen can be detected serologically by the cytotoxicity test *in vitro*.

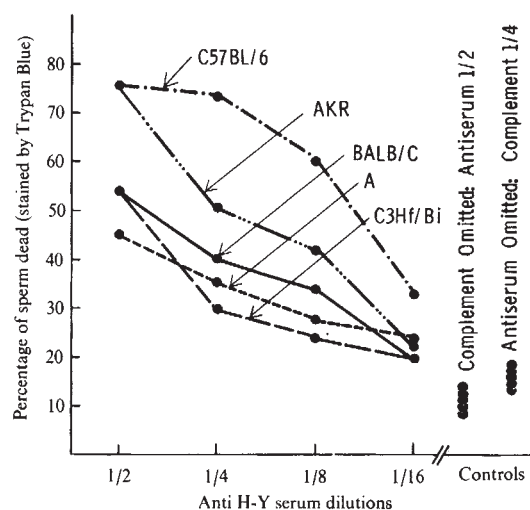


Fig. 1 Detection of H-Y antigen on epididymal sperm of A, C57BL/6, C3Hf/Bi, BALB/c and AKR mice by the cytotoxicity test with serum of C57BL/6 female mice which had rejected C57BL/6 male skin grafts.

(b) H-Y antigen is present on sperm as suggested by indirect evidence *in vivo*⁸. (c) Very probably, at least some X-bearing sperm as well as Y-bearing sperm carry H-Y antigen, indicating that at least some of the surface membrane of sperm is conserved from antecedent cells of an earlier stage in differentiation when both X and Y chromosomes were present in each cell.

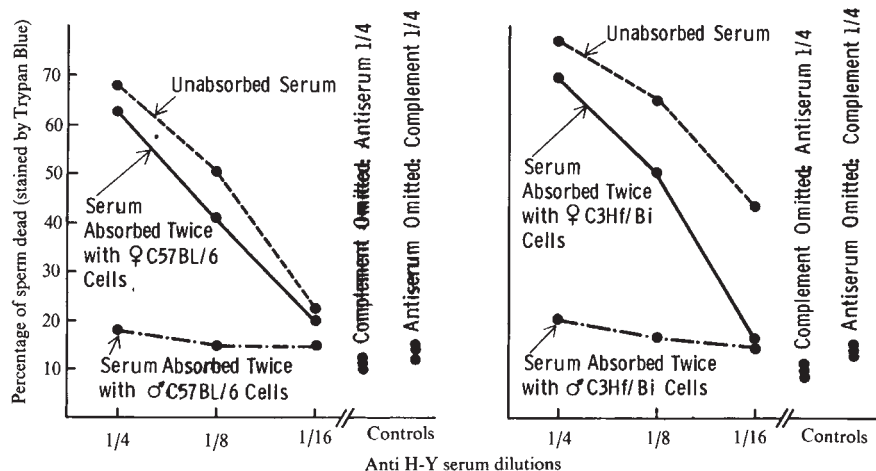
Serum for the cytotoxicity test (referred to as anti H-Y serum) was obtained from C57BL/6 female mice 5–14 days after they had rejected a fourth or fifth skin graft from C57BL/6 males. Complement for the cytotoxicity test was provided in the form of serum from individual rabbits that had been selected for both low toxicity to mouse thymocytes and a high level of complement⁹. Before use, this selected rabbit serum was absorbed twice with mouse cells (eight parts to one by volume), including cells from the testis, in the absence of free calcium, to remove natural hetero-antibody. The object of excluding calcium is to prevent loss of complement during absorption⁹.

freshly prepared solution of trypan blue (stock solution of 1% trypan blue in distilled water, diluted immediately before use with 42.5 g/l. of NaCl, one part in five, to render it isotonic).

The results summarized in Table 1 show that sperm from all strains tested were lysed by anti H-Y serum. Representative tests are illustrated more fully in Fig. 1. Sperm from strains A, C3Hf/Bi and BALB/c were less susceptible than C57BL/6 sperm indicating either (a) that there are strain differences in the amount of H-Y antigen on sperm, or (b) that these strains have different alleles at the H-Y locus¹⁰ so that their H-Y antigens cross-react but are not identical. Known strain differences in rate and incidence of male skin rejection by females may be accounted for on these lines, and this is now amenable to serological investigation.

To confirm that the cytotoxic reaction was specific for H-Y antigen, aliquots of anti H-Y serum (diluted one-quarter) were absorbed twice with equal numbers of either male or female

Fig. 2 Specificity of sperm lysis by anti H-Y serum (1). Titration of cytotoxic anti H-Y serum absorbed twice with either male or female cells, and then tested on C57BL/6 sperm. First experiment (left): absorption with C57BL/6 cells; second experiment (right): absorption with C3Hf/Bi cells.



Mice of the inbred strains C57BL/6, A, AKR, BALB/c and C3Hf/Bi were obtained from colonies maintained by one of us (E. A. B.). Epididymal sperm were obtained by cutting the entire epididymis into slices in a few drops of phosphate-buffered saline (pH 7.0) containing 0.5% fructose and 5% foetal calf serum. After 5 min, the medium containing free sperm was pipetted off and the suspension kept at room temperature until use¹.

Table 1 Cytotoxicity Tests on Mouse Epididymal Sperm with anti H-Y Serum

Strain donating sperm	Experiment							
	(i)	(ii)	(iii)	(iv)	(v)	(vi)	(vii)	(viii)
			% sperm dead	(stained by trypan blue)*				
C57BL/6	71	64	73	81	78	76	88	68
AKR					75			
A	37	57	45	62				
BALB/c	54	55						
C3Hf/Bi	54							

Summary of eight experiments: every test included a control in which complement was omitted and another with antiserum omitted; these showed consistently fewer than 18% sperm dead.

* In antiserum diluted by one half, at which dilution the greatest proportion of sperm were killed (see Fig. 1; undiluted antiserum was not tested).

Doubling dilutions of anti H-Y serum (half to one-sixteenth) were prepared for the cytotoxicity test. Equal volumes (0.05 ml.) of (a) diluted anti H-Y serum, (b) sperm suspension ($4-5 \times 10^6$ /ml.) and (c) absorbed rabbit serum diluted one quarter, were incubated for 45 min at 37° C. Sperm counts were made in a haemocytometer after addition of 0.1 ml. of a

C57BL/6 cells from spleen, lymph node, and thymus (four volumes serum to one volume packed cells for 30 min in an ice bath), and the absorbed sera were then tested on C57BL/6 epididymal sperm. There was only minimal loss of cytotoxic activity after double absorption with female cells, no more than is to be expected from non-specific causes, and essentially complete loss of activity after double absorption with male cells: see Fig. 2, which includes a similar experiment in which C3Hf/Bi cells were used for absorption.

After due allowance for background levels of non-specific death of sperm during the cytotoxicity test, it is clear that the percentage of sperm specifically lysed by anti H-Y serum often exceeds 50. It is probable therefore that as in the case of H-2 (ref. 1) the surface phenotype of at least some sperm reflects the diploid complement of their precursor cells, rather than their own haploid constitution. It must be emphasized that there is no justification for assuming that cells surviving a cytotoxicity test, particularly in a relatively weak system like H-Y, necessarily lack the antigen being tested for; the probability of lysis for each cell of a uniform population probably depends on many randomly variable factors. It would therefore be rash to conclude that the surviving sperm are H-Y⁻.

Anti H-Y sera were not positive in cytotoxicity tests with male thymocytes, lymph node cells or spleen cells. Nevertheless the presence of some H-Y antigen on these cells, or of some H-Y⁺ cells in these populations, is implied by their capacity to absorb H-Y antibody (Fig. 2) and by tests *in vivo*¹¹⁻¹³. In further absorption experiments, we have found that each of these cell populations individually is H-Y⁺; and we shall report elsewhere that the cytotoxicity test is positive with enzymatically dissociated male (but not female) epidermal cells from skin.

E. H. G. is a National Institutes of Health trainee. E. A. B. and E. A. C. were supported in part by a National Cancer Institute grant. D. B. is a career investigator of the Health Research Council of New York and was supported by a National Institutes of Health grant. M. S. was the recipient of a research fellowship from the Stiftung Volkswagenwerk.

ELLEN H. GOLDBERG
EDWARD A. BOYSE
DOROTHEA BENNETT
MARGRIT SCHEID
ELIZABETH A. CARSWELL

Department of Anatomy,
Cornell University Medical College, and
Division of Immunology,
Sloan-Kettering Institute,
New York 10021

Received February 4, 1971.

- ¹ Goldberg, E. H., Aoki, T., Boyse, E. A., and Bennett, D., *Nature*, **228**, 570 (1970).
- ² Vojtiskova, M., Polackova, M., and Pokorna, A., *Folia Biol.*, **15**, 322 (1969).
- ³ Boyse, E. A., Stockert, E., and Old, L. J., *Intern. Convoc. on Immunol.* (Karger-Basel, New York, 1968).
- ⁴ Reif, A. E., and Allen, J. M. V., *J. Exp. Med.*, **120**, 413 (1964).
- ⁵ Boyse, E. A., Miyazawa, M., Aoki, T., and Old, L. J., *Proc. Roy. Soc., B*, **170**, 175 (1968).
- ⁶ Boyse, E. A., and Old, L. J., *Ann. Rev. Genet.*, **3**, 269 (1969).
- ⁷ Eichwald, E. J., and Silmsker, C. R., *Transplant. Bull.*, **2**, 148 (1955).
- ⁸ Katsh, G. F., Talmage, D. W., and Katsh, S., *Science*, **143**, 41 (1964).
- ⁹ Boyse, E. A., Hubbard, L., Stockert, E., and Lamm, M. E., *Transplantation*, **10**, 446 (1970).
- ¹⁰ Hildemann, W. H., and Cooper, E. L., *Transplantation*, **5**, 707 (1967).
- ¹¹ Feldman, M., *Transplant. Bull.*, **5**, 15 (1958).
- ¹² Hirsch, B. B., *Transplant. Bull.*, **4**, 58 (1957).
- ¹³ Billingham, R. E., Silvers, W. K., and Wilson, D. B., *Proc. Roy. Soc., B*, **163**, 61 (1965).

Effects of Steroid Pharmaceuticals on Plasma Zinc

ORAL contraceptives have been found to cause large changes in the levels of copper and iron in the blood¹. Their effects on the level of plasma zinc, however, are uncertain, for although in one case it was reported that the level increased², in another significant decreases were found³. Apart from testosterone propionate, which was found to increase the level of plasma zinc⁴, other widely used steroid pharmaceuticals have not been investigated. We therefore undertook to determine the effects of such substances, including oral contraceptives, on the plasma zinc of healthy human subjects.

All volunteers were free of any obvious disease and were of families with no histories of conditions likely to influence the study. None had taken steroids before. Fasting blood samples were obtained by venepuncture on several occasions before the steroids were taken. No pharmaceuticals, other than the substance under test, were taken during the trial period. For the women in the study, the day of the menstrual cycle was recorded at the collection of each sample.

The steroids and the daily dose levels used were ethinylestradiol (0.05 mg), norethisterone acetate (1.0 and 0.5 mg), ethinylestradiol plus norethisterone acetate ('Minovlar' 0.05 mg + 1.0 mg), *d*(-)-norgestrel (1.0 mg and 0.25 mg), *d*(-)-norgestrel plus ethinylestradiol (Eugynon, 0.25 mg + 0.05 mg), mesterolone (Proviron, 100 mg), and prednisolone (5 mg and 10 mg). The steroids were taken once a day at the same time each day, for 30 consecutive days, except for the oral contraceptives which were taken for 21 days, and for prednisolone which was taken

Table 1 Effects of Steroids on Plasma Zinc

Steroid	Daily oral dose (mg)	Sex	Plasma zinc ($\mu\text{g}/100 \text{ ml.}$, mean $\pm$ s.d.)	P
None	None	F	99 $\pm$ 14	—
None	None	M	98 $\pm$ 15	—
Ethinylestradiol	0.05	F	83 $\pm$ 16	<0.01
Norethisterone acetate	1.0	F	99 $\pm$ 15	N.S.
Norethisterone acetate	5.0	F	89 $\pm$ 15	<0.02
Ethinylestradiol plus norethisterone acetate	0.05+			
<i>d</i> (-)-Norgestrel	1.0	F	82 $\pm$ 15	<0.01
<i>d</i> (-)-Norgestrel	0.25	F	98 $\pm$ 14	N.S.
Ethinylestradiol plus <i>d</i> (-)-norgestrel	0.05+		100 $\pm$ 15	N.S.
Mesterolone	0.25	F	84 $\pm$ 12	<0.01
Prednisolone	100	M	100 $\pm$ 17	N.S.
Prednisolone	5	M	98 $\pm$ 16	N.S.
Prednisolone	10	M + F	101 $\pm$ 15	N.S.

for only 10 days. Twenty-five subjects were investigated, twenty women and five men, ranging in age from 18 to 38 yr. Some received two courses of treatment separated by a suitable interval. Zinc was assayed in plasma by atomic absorption spectrophotometry, using methods similar to those of Davies *et al.*⁵.

The results are given in Table 1. The significance of any changes was assessed by a *t* test of each set of results against the control values. There was no difference in plasma zinc levels between untreated men and women. The stage of the menstrual cycle had no influence on the levels. There was no significant difference between concentrations in blood collected during the follicular or luteal phases, or at the time of menstruation. This finding strongly suggests that changes in endogenous steroid hormones are without effect on plasma zinc. Of the various steroid pharmaceuticals, only oestrogenic preparations had any significant action. Ethinylestradiol, 0.05 mg, given alone or in combination with a progestogen, produced a marked decrease in plasma zinc. This is in contrast to the effect of this steroid on blood iron and copper, both of which are increased¹.

The largest dose of norethisterone acetate (5 mg) also produced a small decrease in plasma zinc; this could be a consequence of the action of oestrogenic metabolites of this progestogen formed *in vitro*. Ethinylestradiol has been identified as a metabolite in the human⁶. That the effect is not due to progestogenic influences is shown by the lack of effect of the other progestogen, norgestrel. The latter is more than five times as progestogenic as norethisterone acetate, but lacks any significant oestrogenic metabolites⁷.

Neither prednisolone nor the oral androgen mesterolone had any effect in contrast to the reported action of testosterone propionate on plasma zinc in rats⁴. To determine whether the action of ethinylestradiol on plasma zinc is reversible, we studied women who had ceased to take the steroid. Normal values were restored after 15 to 20 days. We have also studied levels of plasma zinc in a group of women which had taken oral contraceptives continuously for 5–8 yr. They also showed significantly depressed plasma zinc levels, indicating that the body cannot adopt to exogenous oestrogens and restore the level to normal.

The clinical significance of chronically low plasma zinc is unknown, but zinc has been implicated in a number of liver diseases and in diabetes mellitus. Both these have been suspected as long term side effects of oral contraceptives.

M. H. BRIGGS
MAXINE BRIGGS

University of Zambia,
Lusaka

J. AUSTIN

College of Technology,
Belfast

Received March 10; revised May 4, 1971.

- ¹ Briggs, M. H., *et al.*, *Adv. Steroid Biochem. Pharmacol.*, **2**, 111 (1970).
- ² O'Leary, J. A., and Spellacy, W., *Amer. J. Obstet. Gynecol.*, **103**, 131 (1969).
- ³ Halstead, J. A., and Smith, J. C., *Lancet*, **i**, 322 (1970).
- ⁴ Leonov, V. A., and Dubina, T. L., in *Mikroelm. Biofere* (edit. by Makeev, O. V.), **2**, 562 (Moscow, 1967).
- ⁵ Davies, I. J. T., Musa, M., and Dormandy, T. L., *J. Clin. Pathol.*, **21**, 359 (1968).
- ⁶ Breuer, H., *Intern. J. Fertil.*, **9**, 181 (1964).
- ⁷ Edgren, R. A., *Steroids*, **2**, 319 (1963).

Meiotic Studies of the Ejaculated Seminal Fluid of Humans with Normal Sperm Count and Oligospermia

So far, all known studies of human meiosis have been performed on germinal cells obtained from testicular biopsies^{1,2}. As this involves a surgical procedure to obtain the material, we wish to draw attention to the statement, first made by Michael and Joel³, that immature germ cells can regularly be seen in the seminal fluid of the human male. We have found that in smear preparations of the ejaculate of subjects with a normal sperm count, nearly 3% of the cells consist of spermatogonia, spermatocytes and spermatids (Table 1), the maximum percentage being 5%. A similar result was obtained by Heinke and Doepfmer⁴. As the sperm count decreases, however, the percentage of immature cells generally increases and, in some pathogenic cases, the percentage may be 40% or more⁵. We have characterized the cells in material in which a high percentage of the cells were immature as a preliminary to cytogenetic studies of human male meiosis.

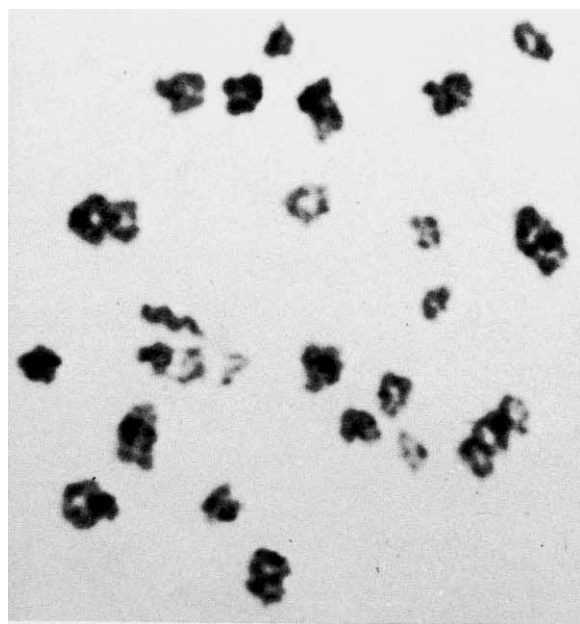


Fig. 1 Primary spermatocyte at diakinesis, from the ejaculated seminal fluid of a human male with oligospermia ($\times 1,800$).

The cells were stained for viability by the trypan-blue method⁶. In both normal and oligospermia seminal fluid,

75–85% of the cells—the viable cells—remained unstained. Furthermore, autoradiographs of spermatogonia and preleptotene spermatocytes indicated that some could incorporate tritiated thymidine. Preparations of the meiotic chromosomes in diakinesis and metaphase-I were made after hypotonic treatment by the air-dry method of Evans *et al.*⁷ (Fig. 1). The best results with cells at the pachytene stage were achieved by the squash method without any pretreatment with the fixative proposed by Annerén *et al.*⁸. The relative frequency of these different stages varies in each case but leptotene and pachytene cells are predominant, possibly because of the long duration of the meiotic prophase⁹. Nevertheless, cells in diakinesis occur in oligospermia preparations and also in the ejaculate of normal males. These preliminary results suggest that the seminal fluid is a useful source of immature germ cells for cytogenetic studies of human male meiosis.

KARL SPERLING
RUDOLF KADEN

*Institute of Genetics, and Department of Dermatology,
Division of Andrology, Free University, Berlin*

Received August 11, 1970.

- ¹ Kjessler, B., in *Modern Trends in Human Genetics* (edit. by Emery, A. E. H.) (Butterworth, London, 1970).
- ² Ohno, S., in *Methoden in der Medizinischen Cytogenetik* (edit. by Schwarzscher, H. G., and Wolf, U.) (Springer, Berlin, 1970).
- ³ Michael, M., and Joel, K., *Schweiz. med. Wschr.*, **33**, 757 (1937).
- ⁴ Heinke, E., and Doepfmer, R., in *Handbuch der Haut- und Geschlechtskrankheiten VI/3* (edit. by Schuermann, H., and Doepfmer, R.) (Springer, Berlin, 1960).
- ⁵ Vasterling, H. W., in *Praktische Spermatologie* (Thieme, Stuttgart, 1960).
- ⁶ Pertoft, H., Bäck, O., and Lindahl-Kiessling, K., *Exp. Cell Res.*, **50**, 355 (1968).
- ⁷ Evans, E. P., Breckon, G., and Ford, C. E., *Cytogenetics*, **3**, 124 (1964).
- ⁸ Annerén, G., Berggren, A., Stahl, Y., and Kjessler, B., *Hereditas*, **64**, 211 (1970).
- ⁹ Heller, C. G., and Clearmont, Y., *Science*, **140** (1963).

Mandibular Gland Secretion of Larvae of the Flour Moth, *Anagasta kuehniella*, contains an Epideictic Pheromone and elicits Oviposition Movements in a Hymenopteran Parasite

Hassell and Huffaker¹ demonstrated some density-dependent regulation of numbers in populations of the flour moth, *Anagasta kuehniella* (Zeller). Fighting between newly hatched larvae² contributes to the regulation of numbers in this species but is not the only controlling mechanism: Smith³ showed that crowding from the end of the first instar onwards led to delayed emergence of adults and a reduction in body weight. Since smaller moths lay few eggs⁴, both these effects would contribute to the density-dependent regulation of numbers in succeeding generations. I describe here a mechanism which could bring about these effects. I suggest that last-instar larvae of *A. kuehniella*, when they meet, deposit on the substratum drops of secretion from their mandibular glands; and that the response of other last-instar larvae to this secretion results not only in the regulation of the total numbers of

Table 1 Mean Percentage of Immature Germ Cells in the Ejaculated Seminal Fluid of Human Males with Different Sperm Qualities

Sperm quality	No. of sperm (million/ml.)	No. of subjects investigated	Spermatogonia (%)	Spermatocytes (%)	Spermatids (%)	Total (%)
Normospermia	≥ 40	139	0.5	0.3	2.0	2.8
Oligospermia I	$\geq 5 < 40$	93	2.0	1.4	4.4	7.8
Oligospermia II	$\geq 1 < 5$	24	7.0	3.4	11.0	21.4

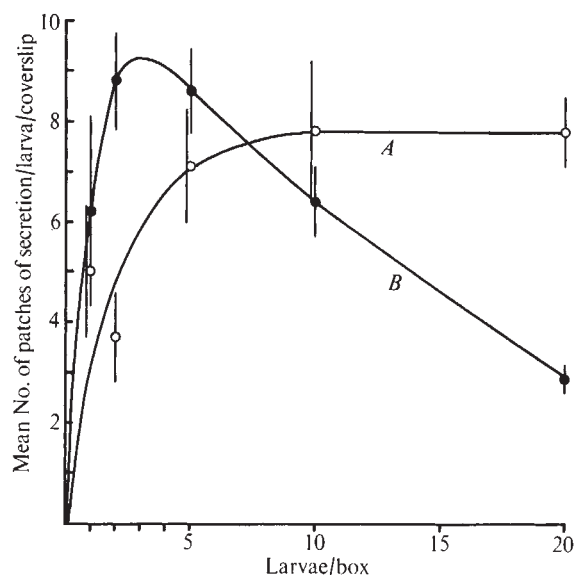


Fig. 1 Mean numbers of patches of mandibular gland secretion per larva on coverslips that were on the floors of boxes in which 1, 2, 5, 10 or 20 larvae were confined for 1 h (A) or for 24 h (B) (experiment 2). Each vertical line represents twice the standard error.

A. kuehniella in a finite system (as studied by Smith³), but also in the control of the dispersion of individuals within that system.

The mandibular glands of last-instar larvae of *A. kuehniella*, like those of *Galleria mellonella* (L.)⁵, are tubular structures lying folded in the haemocoel. One opens at the base of each mandible. They contain a clear oily fluid which is deposited in droplets on the substratum beside the silken thread and can be stained red with Nile blue inside the gland or after deposition. Larvae that meet each other head to head show a characteristic response involving sudden withdrawal and the separation of the mandibles. My experiment 1 showed that this behaviour is sometimes (and perhaps always) accompanied by the release of mandibular gland secretion, which is sometimes deposited on the substratum. In experiment 1A, a larva was allowed to crawl over a 6 cm square surface marked with 1 cm squares, and at recorded locations the withdrawal response was elicited by touching it, head to head, with another larva held in forceps. After three, four or five such encounters the surface was treated with Nile blue and examined for red-staining material. In ten trials of this kind, involving forty-two encounters, all but one of the thirty-six patches of red-staining material were within 1 cm of meeting places or of the places where the larvae were put down at the beginning of each trial; larvae often made the withdrawal response when first put down. Another ten trials (experiment 1B), in which the response was elicited by prodding with forceps instead of by contact with another larva, gave similar results; the larvae were prodded thirty-three times, and all but two of the twenty-three patches of secretion were within 1 cm of a place where a larva had been prodded, or put down at the beginning of a trial. Evidently the withdrawal response, elicited by mechanical stimulation or by contact with another larva, often leads to the deposition on the substratum of secretion from the mandibular glands.

Fig. 1 shows the results of experiment 2 in which larvae were confined for 1 h (A) or 24 h (B), singly or in groups, in standard boxes of internal dimensions 56 × 38 × 13 mm. On the floor of each box was a coverslip (22 × 50 mm) which was subsequently treated with Nile blue so that patches of red-staining secretion on its surface could be counted. The number counted was assumed to be proportional to the number of patches on the inner surfaces of the box. Fig. 1A

shows that individual larvae released more secretion when crowded than when alone, as would be expected if the release of secretion is stimulated by meetings between larvae. Fig. 1B also shows this effect at low densities, although at high densities the number of patches of secretion appears smaller after 24 h than after 1 h, because crowded larvae, walking over the coverslips, picked up the secretion on their bodies. Dissections of larvae that had been crowded for 24 h showed that the percentage with one or both mandibular glands shrivelled and empty increased with the density of crowding from 8% (or 25) for solitary larvae to 48% (or 255) for larvae in groups of twenty per box.

Experiment 3 concerned the response of last-instar larvae of *A. kuehniella* to crowding (3A) and to mandibular gland secretion of other last-instar larvae (3B and C). The response was assessed in terms of the duration of the wandering period, during which fully fed larvae crawl about, away from their food, and which ends with the spinning of the cocoons in which the larvae will pupate. For each experiment a batch of larvae was selected from their stock cultures on the first day of their wandering stage. They were kept in standard transparent boxes at 25 ± 0.5° C and for 10 (3C) or 12 (3A and 3B) days they were examined every morning so that the dates of cocoon-spinning and pupation could be recorded. Individuals (about 1–4%) that failed to spin up during the 10 or 12 day experiments were not included in the results. In each experiment the patterns of variation in the dates of cocoon-spinning and of pupation were alike, and only the dates of pupation are shown here.

In experiment 3A larvae were kept singly or "crowded" in groups of two, five, ten or twenty per box, and the results (Fig. 2A) show a pattern that is repeated in the results of experiments 3B and 3C: the larvae at an intermediate density pupated sooner than those that were either at very low density or very densely crowded. The results of experiment 3B (Fig. 2B) indicate that this effect of crowding was mediated

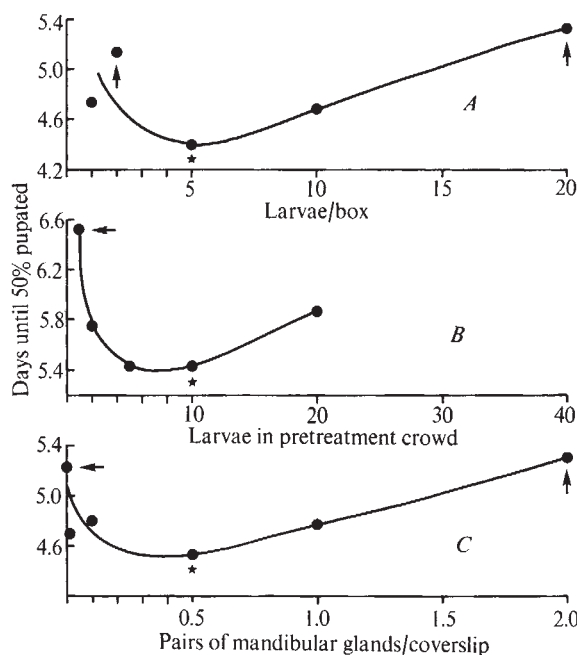


Fig. 2 Results of experiment 3. A, Effect of crowding on the timing of pupation. B, Effect of coverslips, previously exposed to crowds of larvae, on the timing of pupation of isolated larvae. C, Effect of coverslips, treated with ether extract of mandibular glands, on the timing of pupation of isolated larvae. The values on the ordinate are derived from cumulative plots, smoothed by a moving average of three, of the number of new pupae against time. The points marked with a star differ significantly from those marked with an arrow on the same graph ($P < 0.0075$ in A; $P < 0.05$ in B; $P < 0.025$ in C; one-tailed Mann-Whitney U test).

by something deposited on the substratum by crowded larvae. Each larva in this experiment was kept alone in a standard box, on the floor of which was a 22×50 mm coverslip previously exposed for 1 h in a similar box containing one, two, five, ten or twenty larvae (the pre-treatment crowd). Evidently the size of the pre-treatment crowd influenced the timing of pupation of the isolated larvae subsequently exposed to the coverslips, in such a way that pre-treatment crowds of moderate size resulted in earlier pupation than did larger or smaller pre-treatment crowds. The coverslips that had been exposed to these crowds of larvae carried deposits of silk and frass as well as mandibular gland secretion. Experiment 3C provides evidence that it was the mandibular gland secretion that transmitted the crowding stimulus from the pre-treatment crowd to the isolated larvae.

In experiment 3C the larvae were again kept isolated in standard boxes. On the floor of each box was a 22×50 mm coverslip on which had been deposited a drop of ether in which had been ground mandibular glands dissected from last-instar larvae. On the coverslips of the controls drops of pure solvent were deposited. In this experiment (Fig. 2C) changes in the number of pairs of mandibular glands per coverslip affected the timing of pupation as changes in the degree of crowding did: the larvae pupated sooner in the presence of moderate quantities of mandibular glands than they did in the presence of larger or smaller quantities. In one of the three replicates of experiment 3C, each pupa was weighed on its first day after pupation, and the mean weights of the new pupae were calculated for each day. Fig. 3 shows that individuals that pupated later formed lighter pupae than did those pupating earlier.

Experiments 1 and 2 show that the amount of mandibular gland secretion deposited on the substratum is a measure of the density of crowding, and experiment 3 shows that in the presence of appropriate quantities of mandibular gland secretion, isolated larvae responded as though they were crowded. The response mediated by the secretion of the mandibular glands may help to regulate the density towards an "optimal" value, equivalent to about five larvae per box in the conditions of these experiments. Larvae at densities close to this value spin up and pupate relatively quickly, whereas those at higher or lower densities wander for a longer time, thus increasing their chances of reaching an area where the population density is "optimal" before spinning up.

The "overcrowding" effects, expressed by the right hand limbs of the curves in Fig. 2, will regulate the density of the population in three ways: by controlling the spatial distribution of individuals within their habitat, encouraging emigration from crowded situations; by lengthening the generation time of individuals in crowded populations; and by reducing the fecundity of the females crowded as larvae. Fecundity is reduced insofar as wandering larvae spin silk and lose weight as they go, so that those pupating later are, on average, lighter than those pupating earlier (Fig. 3); and lighter flour moths lay fewer eggs than do heavier flour moths⁴. In the presence of the ichneumonid parasite *Venturia canescens* (Grav.) another density-regulating effect comes into play. The mandibular gland secretion of *A. kuehniella* stimulates oviposition movements in the parasite (discussed later), and a larger proportion of the host caterpillars are parasitized in a crowded population than in an uncrowded one⁶.

The secretion of the mandibular glands of *A. kuehniella* falls within the definition of a pheromone given by Karlson and Butenandt⁷. And since it functions in the regulation of population density, controlling the dispersion of individuals, the duration of larval development and the fecundity of the moths, it can be described as an "epideictic"⁸ pheromone.

Venturia canescens, an ichneumonid parasite of *A. kuehniella*, responds to a component of the mandibular gland secretion of its host by making a series of ovipositional movements. When a female of *V. canescens* oviposits in a larva of *A. kuehniella* she taps her antennae against the host, unsheaths

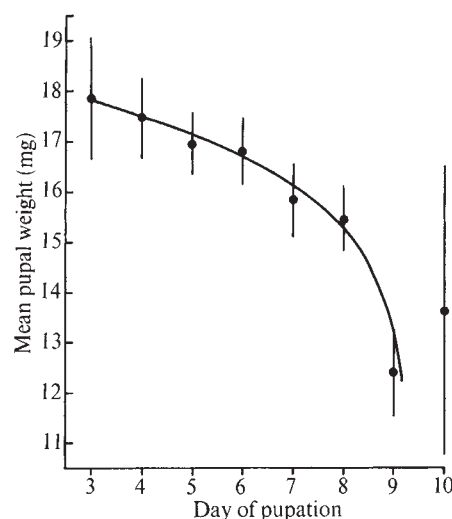


Fig. 3 Mean weights of pupae formed on successive days of experiment 3C. Each vertical line represents twice the standard error.

her ovipositor so that the tip points forwards and downwards, and then makes jabbing movements which, if they penetrate the host's cuticle, may result in the release of an egg. In the absence of a suitable host this series of actions is interrupted at some point before the release of the egg. In my experiments between thirty and fifty adult females of *V. canescens* were confined in a dish with a small rectangle of filter paper to which the materials under test had been applied as two spots placed symmetrically about 2.5 cm apart. For 10 min I recorded the number of "jabbing sessions" directed at each spot. A "jabbing session" involved unsheathing the ovipositor, making one or more jabbing movements, and returning the ovipositor to its resting position. For each of the ten trials in experiment 4A, five last-instar larvae of *A. kuehniella* were separated into (i) the heads with the mandibular glands and the silk glands attached, and (ii) the rest of the bodies. The two spots presented to the parasites consisted of breis made from these two portions of the larvae. Ninety-two per cent of the parasites' jabbing sessions were directed at the spots containing the heads, mandibular glands and silk glands (Table 1). In each of the ten trials in experiment 4B one crushed pair of mandibular glands was tested against the crushed pair of silk glands from the same last-instar larva. (The head, contaminated with the products of both glands, was discarded.) The mandibular glands elicited 95% of the jabbing sessions (Table 1).

Table 1 Results of Experiment 4

	Material presented to parasites	No. of jabbing sessions
A	Head + glands of <i>A. kuehniella</i> larvae	784 (92%)
	Rest of bodies of <i>A. kuehniella</i> larvae	69 (8%)
B	Mandibular glands of <i>A. kuehniella</i> larva	530 (95%)
	Silk glands of <i>A. kuehniella</i> larva	27 (5%)

These two experiments indicate that the contents of the mandibular glands elicit jabbing by the parasites. If a coverslip is exposed to a crowd of host larvae, droplets of mandibular gland secretion are deposited on it (experiment 2). Experiment 4C shows that coverslips treated in this way elicit jabbing by the parasites, and that the number of jabbing sessions directed at a coverslip depends on the number of host larvae to which that coverslip was previously exposed. In each of the ten trials of experiment 4C, 22 mm square coverslips were put on the floor of four standard boxes containing, respectively, one, five, ten and twenty wandering last-instar larvae

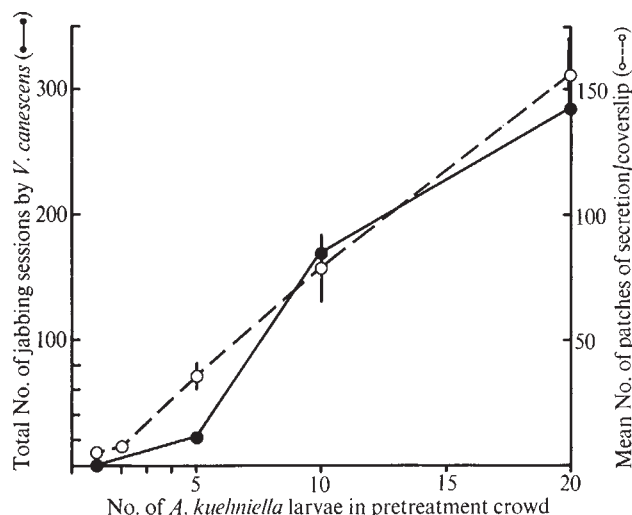


Fig. 4 ●, Effect of pre-treatment of 22 mm square coverslips by exposure for 1 h to larvae of *A. kuehniella* in eliciting jabbing by *V. canescens* (experiment 4C). ○, Mean numbers of patches of secretion deposited on 50×22 mm coverslips by larvae of *A. kuehniella* during one hour's pre-treatment (experiment 2). Vertical lines represent twice the standard error.

of *A. kuehniella*. After 1 h at 25° C the four coverslips were removed, arranged in a square and presented simultaneously to between thirty and fifty adult females of *V. canescens* trapped under an inverted glass dish. The number of jabbing sessions directed at each coverslip was recorded during 10 min. The summed results of the ten trials are shown in Fig. 4.

These experiments show that the parasite *V. canescens* responds quantitatively to the secretion of its hosts' mandibular glands, which carries an intraspecific message announcing crowding; the secretion contains material which is, from the parasites' point of view, a kairomone⁹. This case parallels the situation in which the predatory beetle *Thanasimus dubius* (F.) responds to a supposed aggregation pheromone of its prey, the bark beetle *Dendroctonus frontalis* Zimm.¹⁰. Similar responses of hymenopteran parasites to the mandibular gland secretions of their lepidopteran hosts may occur in other species; *Cardiophiles nigriceps* Viereck, a hymenopteran parasite of *Heliothis virescens* (F.), shows a searching response in the presence of the secretion of the larval mandibular glands of its hosts¹¹.

The finding of an epideictic pheromone in the secretion of the mandibular glands of *A. kuehniella* may be applicable in the control of lepidopteran pests, especially if the mandibular glands of other species prove to have a similar function¹². Work is in progress on the chemical characterization of the components of the secretion, making use of the parasites' ovipositional response as a bioassay for the kairomone.

I thank Dr Philip S. Corbet, Professor J. Green, Dr P. A. Lawrence and Professor V. C. Wynne-Edwards for helpful comments.

SARAH A. CORBET

Westfield College (University of London),
London NW3

Received February 1; revised March 30, 1971.

¹ Hassell, M. P., and Huffaker, C. B., *Researches Popul. Ecol. Kyoto Univ.*, **11**, 186 (1969).

² Flanders, S. E., *Hilgardia*, **39**, 367 (1968).

³ Smith, S. D., *J. Exp. Zool.*, **170**, 193 (1969).

⁴ Ulyett, G. C., and Merwe, J. S. v. Jd., *J. Entomol. Soc. South Africa*, **10**, 46 (1947).

⁵ Wroniszewska, A., *J. Insect Physiol.*, **12**, 509 (1966).

⁶ Hassell, M. P., *J. Anim. Ecol.*, **40**, 333 (1971).

⁷ Karlson, P., and Butenandt, A., *Ann. Rev. Entomol.*, **4**, 39 (1959).

⁸ Wynne-Edwards, V. C., *Animal Dispersion in Relation to Social Behaviour* (Oliver and Boyd, Edinburgh and London, 1962).

⁹ Brown, jun., W. L., Eisner, T., and Whittaker, R. H., *Bioscience*, **20**, 21 (1970).

¹⁰ Vité, J. P., and Williamson, D. L., *J. Insect Physiol.*, **16**, 233 (1970).

¹¹ Vinson, S. B., *Ann. Entomol. Soc. Amer.*, **61**, 8 (1968).

¹² *ITBON in 1965*, Annual Report of Institute for Biological Field Research, Arnhem, Netherlands.

Presumptive X Monosomy in Black Rats from Malaya

DURING a cytogenetic study of the Malayan species of *Rattus* Fischer, black rats, *Rattus rattus diardii* (Jentink), were trapped at Kuala Lumpur, Selangor, and Batu Pahat, Johore, between November 1968 and July 1970. Ninety animals were examined cytologically and seventeen gave chromosome counts that differed from the normal diploid number of 42 (ref. 1). Fourteen had between one and three additional small metacentric chromosomes which were not distinguished from normal members of the complement. Nevertheless, they are assumed to be equivalent to the "inert" supernumerary (or B) chromosomes of many invertebrate and plant species. Counts of 41 chromosomes were recorded repeatedly in preparations from four of the rats trapped at Kuala Lumpur. Karyotype analysis indicated that "Robertsonian fusion" between two acrocentric chromosomes had occurred in a male specimen². In the remaining three specimens (all females) an acrocentric chromosome was absent. Observations were made on preparations from bone marrow.

Apparent monosomy was a surprising observation, and so these preparations were re-evaluated. From each animal twenty well spread metaphases were selected at low magnification and counted at high magnification by the sector method (which has the advantage that whatever errors may be made in interpretation the final count recorded is not influenced by prior knowledge of an "expected" number). The results confirmed previous counts. As a further precaution the preparations were sent to another laboratory, where the diploid number was verified to be 41 in all three animals.

Only the two longest and perhaps the shortest of the 11 pairs of acrocentric autosomes can be distinguished individually. The remainder, together with the X chromosome, which is also acrocentric, are difficult to separate by size³. It is therefore significant that the three animals were all females, and the most reasonable assumption is that all were X monosomics. Autopsy of one revealed normal ovaries, uterus and other female reproductive organs, but this is not an inconsistent observation since XO female mice are both viable and fertile⁴.

The alternative interpretation of autosomal monosomy is highly unlikely. In man several examples of autosomal monosomy have been reported in cultures established from spontaneously aborted fetuses. They are, however, rare in comparison with the numbers of autosomal trisomies identified (theoretically, near equality in numbers is expected in the zygote population). In the one case of a live-born infant reported with non-mosaic monosomy-G⁵, conservation of a normal or near normal genome by translocation to another site cannot be excluded on the evidence presented. In the mouse, new evidence indicates that autosomal monosomies may develop normally up to the blastocyst stage and even implant, but all die before the tenth day of gestation (personal communication from C. E. Ford).

In the marsupial genera *Isoodon*, *Perameles*, *Echymipera* and *Peroryctes*, loss of one X chromosome in females or of the Y chromosome in males is a normal event in many somatic tissues though not in the germ cells, which retain the zygotic XX and XY constitution respectively^{6,7}. A single field mouse, *Akodon azarae*, had also been reported to possess an XO sex chromosome complement at least in the somatic tissues⁸.

Since bone marrow was the only tissue studied in the three *R. rattus* monosomics the possibility has to be borne in mind that the loss of the one chromosome may have been confined to bone marrow and perhaps other somatic tissues. If it were so it would imply a labile system of regulation of sex chromosome loss, operative in a small proportion of animals.

Whatever the explanation, *X* monosomy, an *Isodon/Perameles*-like system or even autosomal monosomy, the observation is unexpected, leaving many questions to be answered.

I thank Dr C. E. Ford for his interest, and for verifying my chromosome counts.

YONG HOI-SEN

Division of Genetics,
School of Biological Sciences,
University of Malaya,
Kuala Lumpur

Received May 18, 1971.

¹ Yong, H. S., *Third Oxford Chromosome Conference* (1970).

² Yong, H. S., *Experientia*, **27**, 467 (1971).

³ Yong, H. S., *Chromosoma*, **27**, 245 (1969).

⁴ Cattanaich, B. M., *Genet. Res. Camb.*, **3**, 487 (1962).

⁵ Al-Aish, M. S., de la Cruz, F., Goldsmith, L. A., Volpe, J., Mella, G., and Robinson, J. C., *New Engl. J. Med.*, **277**, 777 (1967).

⁶ Hayman, D. L., and Martin, P. G., *Genetics*, **52**, 1201 (1965).

⁷ Hayman, D. L., Martin, P. G., and Waller, P. F., *Chromosoma*, **27**, 371 (1969).

⁸ Bianchi, N. O., and Contreras, J. R., *Cytogenetics*, **6**, 306 (1967).

Frequency of Blood Feeding in the Mosquito *Aedes aegypti*

THE probability that a female mosquito transmits a pathogen from one host to another depends, in part, on the frequency of blood feeding. *Aedes aegypti* (L.) is a vector of several arboviruses, whose feeding frequency has been measured in the laboratory¹⁻⁴. We now present a direct field estimate of this parameter.

Subject to several assumptions⁵, the chief population parameters can be estimated by marking, releasing and recapturing individual animals of a population in its natural habitat. It is essential that marked and unmarked individuals have equal probabilities of being captured⁶. An adult female mosquito, however, repeatedly passes through a sequence of behavioural phases such as feeding, resting and oviposition, and no sampling method is known that would confer an equal probability of capture on individuals in these different phases. These disadvantages were largely avoided in our study which also enabled the frequency of blood feeding to be estimated.

The catching area was in the centre of a tree-shaded scrap heap of old motor cars in a suburb of Dar es Salaam (6° 49' S, 39° 15' E), on the coast of Tanzania. Large piles of rainwater-filled tyres provided a habitat for a large breeding population of *A. aegypti*. Female mosquitoes which showed attempted biting behaviour were caught by a team of four men during a 5 h period from dawn onwards, on twenty-three consecutive days from June 4, 1970. During the first 11 days (except day 1) captured *A. aegypti* females were checked for marks and given an opportunity to engorge on the experimenters. Fully engorged females, and others bearing a mark, were then lightly etherized and each painted with a single date code mark on the thorax; the technique causes no apparent harm^{7,8}. After marking, the females were released at the capture site and most dispersed in the manner typical after feeding. Females not so released were killed. After the eleventh day, captured mosquitoes were merely preserved for checking. All marks were made and interpreted by one of us (G. A. H. McC.).

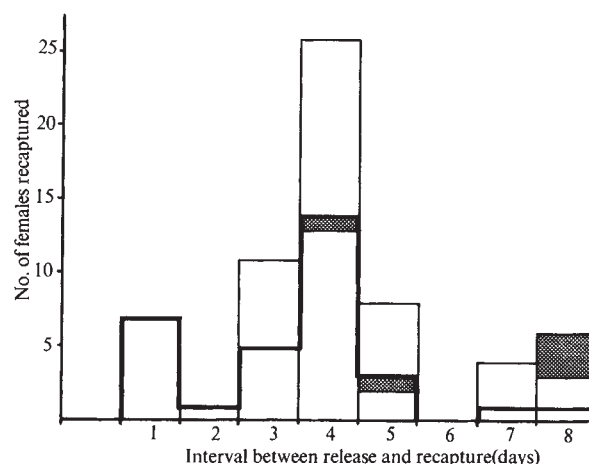


Fig. 1 The results of the mark-release and recapture of females of *Aedes aegypti* during 23 days in Buguruni, Tanzania, expressed as a frequency histogram of the intervals between release and recapture. The area below the heavy line represents females that were released after engorgement and which engorged within 6 h after recapture. The hatched portions of the columns refer to intervals between first release and second recapture for females recaptured twice.

The gross loss on capture of the 579 females caught during the first 11 days was 19.2% and included three which bore a mark from a previous day. Only 1.3% of the 474 females which engorged could not be released after handling. Of 418 singly marked females released, fifty-three were recaptured; fifty of these were released with two marks and, of these, five were recaptured. Because the difference between these recapture rates is insignificant ($\chi^2(1) = 0.30$) data from singly and doubly marked females can be combined. The total of fifty-eight recaptures is 12.4% of the 468 females released. In an open environment this recapture rate is unexpectedly high. In a similar, though longer term, experiment in Thailand on a population of *A. aegypti*, sampled indoors, the recapture rate was only about 4% (ref. 8).

Fig. 1 indicates the frequency distribution of the numbers of females recaptured at various intervals since the date of release. For the five individuals recaptured twice, the intervals between each release and recapture as well as the overall interval are recorded separately. The fifty-eight recaptures therefore provide data for sixty-three release-recapture intervals. After deducting females dying or refusing blood and those caught after day 11, there remain thirty-three unequivocal intervals between engorgements (depicted by the heavy line in Fig. 1). It must be emphasized, however, that some females probably took additional blood meals between the known engorgements at release and recapture.

The striking 4 day modality is clearly an indication of the gonotrophic cycle at the mean air temperature of about 24° C which prevailed during the study. The average intervals between feeding recorded in the laboratory have varied from 3 to 5 days¹⁻⁴.

At least half the females in laboratory populations have been reported to feed on the second as well as on the first day of the gonotrophic cycle^{2,3}. In the field, several workers⁸⁻¹⁰ have discovered that a considerable proportion of biting females were already blood-fed, gravid or partially gravid with sufficient blood to complete ovarian development. It has been suggested⁹ that double feeding, in the first gonotrophic cycle, is a response to inadequate larval nutrition. The data reported here, however, not only confirm double feeding in seven individuals recaptured 24 h after release, but, because one of these was recaptured 4 days after initial release and again on day 5, they also imply double feeding in a subsequent gonotrophic cycle.

In Fig. 1 the recaptures at 3, 5 and 7 days can be regarded as deviations from a 4 day mean, with the first day recaptures indicating double feeds in the first gonotrophic cycle only. The results could equally be interpreted, however, as representing an invariable 4 day cycle with a second feed after 1 day in each cycle. With this interpretation the intervals of 3 and 7 days are derived from individuals initially captured as "second feeders" and recaptured taking the first feed of a subsequent cycle. The 5 day intervals are derived from females caught as "first feeders" and recaptured as "second feeders" in the next cycle. The occurrence of a fairly high frequency of double feeding in *A. aegypti* implies that it can be an effective vector of viruses both at lower densities and, if the interpretation of double feeding in later gonotrophic cycles is correct, at lower survival rates than have hitherto been realized.

This study was supported jointly by a US Public Health Service research grant from the Center for Disease Control, Atlanta, Georgia, and the World Health Organization. We thank Dr W. K. Hartberg for his assistance and Mr J. W. Wright and Dr A. W. A. Brown for their interest and support.

G. A. H. McCLELLAND

Department of Entomology,
University of California,
Davis, California 95616

G. R. CONWAY

Environmental Resource Management Research Unit,
Imperial College of Science and Technology,
Silwood Park, Ascot, Berkshire

Received March 8; revised April 14, 1971.

- ¹ Macfie, J. W. S., *Bull. Ent. Res.*, **6**, 205 (1915).
- ² Lavoipierre, M. M. J., *Nature*, **181**, 1781 (1958).
- ³ Judson, C. L., *Biol. Bull.*, **133**, 369 (1967).
- ⁴ Gillett, J. D., *J. Insect. Phys.*, **8**, 665 (1962).
- ⁵ Southwood, T. R. E., *Ecological Methods* (Methuen, London, 1966).
- ⁶ Jolly, G. M., *Biometrika*, **52**, 225 (1965).
- ⁷ Macdonald, W. W., Sebastian, A., and Maung-maung-Tun, *Ann. Trop. Med. Parasit.*, **62**, 200 (1968).
- ⁸ Sheppard, P. M., Macdonald, W. W., Tonn, R. J., and Grab, B., *J. Anim. Ecol.*, **38**, 661 (1969).
- ⁹ Macdonald, W. W., *Ann. Trop. Med. Parasitol.*, **50**, 399 (1956).
- ¹⁰ Gould, D. J., Mount, G. A., Scanlon, J. E., Ford, H. R., and Sullivan, M. F., *J. Med. Entomol.*, **7**, 499 (1970).

Synthetic Mimics of Insect Juvenile Hormone

TERPENE derivatives other than farnesol possess excellent juvenoid activity¹. We have examined the effects of epoxidized and unepoxidized aromatic ethers of geraniol on yellow mealworm (*Tenebrio molitor*), confused flour beetle (*Tribolium confusum*) and other insects. The compounds can be synthesized easily from commercial materials and are reasonably stable to sunlight and hydrolysis. We have investigated the relationship between their chemical structures and their biological activity in the yellow mealworm².

Table 1 Juvenile Hormone Activity of Certain Para-substituted Phenyl Geranyl Ether Compounds on *Tenebrio molitor* Pupae

		ED-50 (μg/pupa) *			
	Code	n=0	Code	n=1	n=0/n=1
CH ₃ -	I	1.0	II	0.05	20.0
C ₂ H ₅ -	III	0.1	IV	0.0025	40.0
n-C ₃ H ₇ -	V	> 0.5	VI	0.1	> 5.0
i-C ₃ H ₇ -	VII	0.8	VIII	0.01	80.0
CH ₃ O-	IX	1.5	X	1.0	1.5
C ₂ H ₅ O-	XI	5.0	XII	0.2	25.0
CH ₃ S-	XIII	0.2	XIV	0.03	6.7
<i>Cecropia</i> hormone †			XV	3.0	

* Effective dose causing abnormal development of 50% of treated pupae.

† Methyl *cis*-10-epoxy-7-ethyl-3,11-dimethyl-*trans,trans*-2,6-tridecadienoate is included for comparison, and was kindly supplied by W. S. Bowers, USDA, Beltsville, Maryland.

Candidate compounds were applied topically in 1 μl. of acetone to the venter of newly formed *Tenebrio molitor* pupae, which were then incubated at 28° C and 75% relative humidity for 7 days. Signs of abnormal development included retention of urogomphi, gin traps, and general appearance of a pupal-adult intermediate³⁻⁵.

Test compounds were synthesized from geranyl bromide by treatment with *m*-chloroperbenzoic acid to form the epoxide, which was then reacted with phenol in 1,2-dimethoxyethane in the presence of powdered potassium hydroxide. Geranyl bromide was used directly in the ether synthesis of the unepoxidized compounds. Structures were confirmed by infrared and mass spectroscopy and by nuclear magnetic resonance.

The activities of fourteen compounds in the *Tenebrio* test are given in Table 1. Seven epoxidized and unepoxidized compounds were compared for morphogenetic activity. The epoxidized forms (VIII) always had a higher order of activity¹, ranging up to eighty times that of the unepoxidized structure (VII). Compound IV, with an ethyl substituent on the phenyl ring, had the greatest activity, and all the compounds were significantly more active than the *Cecropia* hormone (XV), IV being 1,000 times more active than XV.

Compound IV was also tested on a stored product pest, *Tribolium confusum*, to demonstrate the feasibility of pest control by hormones. Twenty adult beetles were placed in glass bottles containing 100 g of flour that had been mixed with compound IV in concentrations varying from 0.01 to 1,000 p.p.m. Untreated flour was fed to control beetles. The results are given in Table 2. Adult development of *Tribolium confusum* was completely arrested by 10 p.p.m. or more and newly formed adults died prematurely even when the compound was present at the lowest test concentration—0.01 p.p.m. Survival of the original twenty adults in the presence of the

Table 2 Effect of Compound IV on *Tribolium confusum* Populations grown in Treated Flour

Life stages present 120 days after treatment		Concentration in flour (p.p.m.)					
		0	0.01	0.1	1	10	100
Adults:	No. alive	600	286	180	57	20	20
	No. dead	6	264	120	93	0	0
Pupae		+++	+++	+++	+++	+++	+
Larvae		+++	+++	+++	+++	+++	+
Supernumerary larvae		0	0	0	+	+++	+++
Adult-pupal intermediates		0	0	0	0	+	+

0 = none; + = few; ++ = moderate; +++ = many.

highest test concentration (1,000 p.p.m.) eliminated the possibility of direct toxicity of IV to the test insects. The activity of compound IV was superior to MTDD (3,7,11-trimethyl-7,11-dichloro-2-dodecenoate) which arrested development of *T. castaneum* at 100 p.p.m. in the flour diet⁶.

These results suggest that stored product pests could be controlled by compounds possessing juvenile hormone activity. They also suggest that compound IV exerts its morphogenetic action through contact and/or ingestion. Compound IV is being tested in other laboratories and already the data indicate morphogenetic and sterilant effects in a variety of insect species including mosquito, tobacco budworm, cotton boll weevil, Indian-meal moth, stable flies, livestock ticks and body lice. Rats, on the other hand, seem to be unaffected by compound IV: when dosed orally with 4,000 mg kg⁻¹, no adverse effects were observed during a 14 day observation period.

Bearing the potential of these chemicals as pest control agents in mind, tests were conducted to obtain information on the influence of environmental factors on their chemical stability. Compound IV was spread in thin films on glass plates to determine the effects of light and air on stability, and known amounts were suspended in tap water to determine hydrolytic effects. At the end of each exposure, compound IV was rinsed off the glass plates with acetone or extracted from water and appropriate aliquots were bioassayed in the *Tenebrio* test. These tests indicated that compound IV is stable to sunlight and air for at least 12 h and that it does not hydrolyse in water in 24 h. These results are encouraging since they indicate that these mimics of juvenile hormones are sufficiently stable to act in a natural environment.

We thank H. Lee, K. Tseng and F. Kamienski for technical assistance.

FERENC M. PALLOS

Stauffer Chemical Company,
Western Research Center,
Richmond, California 94804

JULIUS J. MENN
PETER E. LETCHWORTH
JOHN B. MIAULLIS

Stauffer Chemical Company,
Agricultural Research Center,
Mountain View, California 94040

Received February 1; revised April 7, 1971.

¹ Bowers, W. S., *Science*, **164**, 323 (1969).

² Stauffer Chemical, Belgian Patent 734,904 (1969).

³ Bowers, W. S., and Thompson, M. J., *Science*, **142**, 1469 (1963).

⁴ Bowers, W. S., *Science*, **161**, 895 (1968).

⁵ Chase, A. M., *Nature*, **215**, 1516 (1967).

⁶ Thomas, P. J., and Bhatnagar-Thomas, P. L., *Nature*, **219**, 949 (1968).

Natural Selection and the Evolution of Proteins

Jukes and King¹ have attacked my article². They do not quote my published criticism of their arguments³. Many of the points are discussed therein, and so a detailed reply is hardly necessary. They do, however, raise one additional matter of importance. They maintain that a selectionist hypothesis would predict radical changes to be favoured over conservative changes. The compelling arguments against this interpretation were clearly stated by Fisher in 1930 (ref. 4). He demonstrated that selection is very unlikely to favour extreme changes.

BRYAN CLARKE

Genetics Laboratory,
School of Botany and Zoology,
University Park,
Nottingham NG7 2RD

Received June 6, 1971.

¹ Jukes, T. H., and King, J. L., *Nature*, **231**, 114 (1971).

² Clarke, B., *Nature*, **228**, 159 (1970).

³ Clarke, B., *Science*, **168**, 1009 (1970).

⁴ Fisher, R. A., *The Genetical Theory of Natural Selection* (Oxford University Press, London, 1930).

Deepest Photographic Evidence of an Abyssal Cephalopod

THE bathymetric distribution of marine organisms collected during oceanographic expeditions is often difficult to ascertain because retrieval methods (nets, dredges, and so on) do not always indicate the precise depth at which an organism is entrapped. The level at which organisms dwell can, however, be accurately defined by deep ocean bottom photography.

On a recent Caribbean cruise of USNS Lynch, 340 exposures of the sea floor were obtained at seventeen stations. A modified Alpine multi-exposure camera system was used consisting of two 35 mm cameras mounted on a single frame and actuated by a bottom contact switch. Both cameras utilized the Hopkins water corrected 33 mm f/4.5 lenses. An oblique view of the ocean floor was obtained by tilting the lower camera's viewing angle to 40° with respect to the camera frame.

Among the records was the deepest photographic observation yet made of a marine cephalopod¹, a benthic species belonging to the family Cirroteuthidae (Fig. 1). Except for the thin web which unites all arms for part of their length, much of the



Fig. 1 Ocean bottom photograph of a cephalopod belonging to the family Cirroteuthidae. Taken 325 miles north-east of Barbados in an Abyssal Hill Province at station Lynch 33-14, latitude 17° 28.7' N, longitude 56° 13' W, depth 5,145 m on April 12, 1970. The specimen is approximately 1 m above the ocean floor.

external appearance of the octopod is visible. One of the obovate dorsal fins which assist the organism in balance and orientation can be seen, and also the eye, the dark spot located just above the arms. The estimated total length of the specimen is 45 cm.

The specimen may either have entered the camera's field of view from above, or more probably was startled by the camera's intrusion and is seen ascending in an escape reaction. The apparent absence of disturbed sediment would indicate that it was not lying on the sea floor. The sea floor at the camera station is fairly smooth, though numerous small lumps, depressions and oblate mounds are present. A sediment core taken simultaneously with the camera drop reveals the top 20 cm to be a brown slightly calcareous lutite. The potential temperature of the bottom water is 1.4° C (Escowitz and Amos, in preparation).

I thank G. L. Johnson and W. Ruddiman for their help and technical assistance, C. Roper at the Smithsonian Institution for identifying the specimen, and Captain J. Hobbs, the crew of the USNS Lynch and participating Navocean personnel.

W. JAHN

Code 7400,
US Naval Oceanographic Office,
Suitland, Maryland 20390

Received April 28, 1971.

¹ Roper, C. F. E., and Brundage, W. L., *Ocean Industry Magazine*, April, 52, 54 (1970).

Skeleton of a Late Glacial Elk associated with Barbed Points from Poulton-le-Fylde, Lancashire

THE almost complete skeleton of an elk or moose (*Alces alces* L.) associated with two uniserial barbed points of bone or antler has recently been recovered from one horizon of a series of freshwater deposits revealed by the digging of foundations at High Furlong, Poulton-le-Fylde, Lancashire (NGR SD/3312 3867). An archaeological excavation subsequent to the discovery revealed *in situ* the hind parts of the skeleton and the second barbed point. Stratigraphic data were recorded, and samples were obtained for palaeoecology and dating.

The site lies near the 50' contour, about 2 miles north-east of Blackpool. Borings were made at regular intervals along an approximately east-west line produced from the face of the cutting in which the skeleton and artefacts were found. These revealed a local depression in the till surface, approximately 40 m from east to west, in which limnic deposits of sands, clays and peats had accumulated. The basin extended in a north-south direction for at least 12 m, but building development in the area made its full extent difficult to determine.

The stratigraphy recorded close to the elk remains was as follows. (Datum was 36 cm below present ground level and 13.47 m above OD.)



Fig. 1 Left metatarsal showing a lesion caused by one of the barbed points.

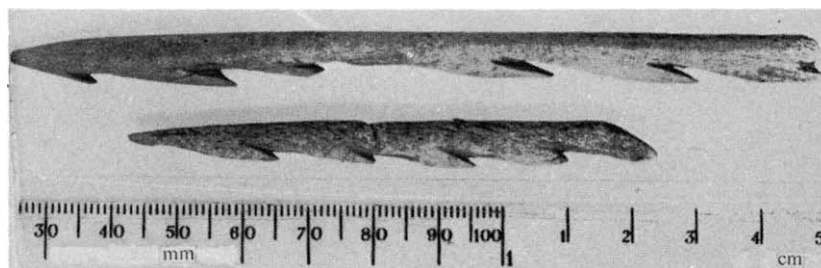
- 0- 12 cm Clayey soil
- 12- 28 cm Carr peat with *Betula* wood throughout, *Phragmites* leaves and *Potamogeton* fruitstones at base, and *Sphagnum* above 17 cm
- 28- 31 cm Grey sandy mud with frost-shattered stones to 3 cm
- 31- 45 cm Silty muddy clay
- 45- 55 cm Dark grey clay with stones to 5 cm
- 55- 64 cm Coarse detritus mud with *Potamogeton* and freshwater bivalve molluscs; elk bones in this horizon
- 64- 97 cm Olive-grey calcareous shelly gyttja
- 97-104 cm Clay with monocotyledonous fragments
- 104-123 cm Red-grey thixotropic clay
- 123-125 cm Sandy clay
- 125-127 cm Sand with gravel to 5 cm

Nine metres west of this point, close to the centre of sedimentation, the same stratigraphic units attained a total thickness of 270 cm.

The sediments are clearly of freshwater origin. The stratigraphic sequence of clays sandwiching organic gyttja is reminiscent of the familiar "Allerød oscillation" of late Weichselian age noted at other sites in lowland Lancashire^{1,2,4} and elsewhere in north-west Europe. Pollen analysis confirms that the deposits from 28 to 104 cm in the profile date from zones I, II and III of the conventional British pollen zone sequence. It is, therefore, unlikely that the age of the elk skeleton is less than 10,800 radiocarbon years BP³.

The skeleton is that of a male elk, and is almost complete, lacking only the left maxillary teeth, part of the left maxilla, the caudal vertebrae, some carpals and parts of the ribs and

Fig. 2 The barbed points.



sternum. It bears numerous lesions (Fig. 1), and these, together with the presence of two barbed points (Fig. 2) in association with the bones, make it clear that the animal had been attacked by hunters.

The two barbed points, which are very similar, are made from either bone or antler. Both have their basal ends missing; one is 12.3 cm long and the other, found lying in two halves across the base of the left metatarsal of the elk, is 8.0 cm long. Typologically, they are more closely related to the early Mesolithic Magdalenian cultures than to the upper or epi-Palaeolithic Magdalenian or Ahrensburgian. The zone II dating of the horizon in which they were found, however, places them chronologically in the epi-Palaeolithic phase, thus providing a rare link between the cultures of the late Glacial and early Boreal periods.

The original discovery of the skeleton was made by Mr. T. Scholey and Mr. J. Audus. The archaeology is being carried out by J. S. H., and B. J. N. E.; stratigraphic evidence is being studied by B. B., who thanks Professor F. Oldfield for his assistance; and the skeleton is under study by A. J. S. A detailed report is in preparation.

B. BARNES

Poulton-le-Fylde College of Education

B. J. N. EDWARDS

Lancashire Record Office, Lancaster Road, Preston

J. S. HALLAM

A. J. STUART

Department of Geology, University of Manchester

Received March 10, 1971.

¹ Birks, H. J. B., *New Phytol.*, **64**, 270 (1965).

² Godwin, M., *Phil. Trans. Roy. Soc.*, **B**, **242**, 127 (1959).

³ Godwin, M., Walker, D., and Willis, E. H., *Proc. Roy. Soc.*, **B**, **150**, 199 (1957).

⁴ Oldfield, F., *New Phytol.*, **59**, 192 (1960).

Relationships of *Amphipithecus* and *Oligopithecus*

A RECENT article by Szalay¹ could be taken to be a definitive statement of the relationships of two of the earliest known specimens that can possibly be related to the origin of the catarrhine primates, the group which includes Old World monkeys, apes and men. Each of the fossils concerned—*Amphipithecus* from the late Eocene of Burma and *Oligopithecus* from the Oligocene exposures in the Fayum, Egypt—is known only from a single specimen. A different assessment of their relationships is presented here. Colbert has already shown^{2,3} clearly and competently why the teeth and tooth cusps of *Amphipithecus* resemble those of catarrhines. I here outline some observations on how jaws function and why and how the jaw of *Amphipithecus* can be demonstrated to be similar to or different from those of other animals.

There has been much debate about the affinities of *Amphipithecus* as is shown by the following summary: (1) Colbert judged² the fragment of this animal—a jaw which contains P₃, P₄, M₁ and roots of P₂ and the canine—to be a probable member of Anthroproidea (the higher Primates) and he emphasized³ further that this species could be excluded from significant relationship to extinct lemuroids or other lower primates. (2) Piveteau suggested⁴ that *Amphipithecus* might either be a relative of South American monkeys (seemingly unaware how surprising its presence in Asia would be), or if not a platyrrhine it was perhaps not a primate at all. (3) Hürzeler found⁵ the animal impossible to classify. (4) Remane assessed⁶ the animal as standing between lower and higher Primates. (5) von Koenigswald thought⁷ it likely to be a lemuroid, but later suggested⁸ that it should be cast out of the Primates into the archaic mammalian order Condylarthra (a group of mammals, incidentally, not otherwise found in Burma or elsewhere in Asia). (6) I then repeated that if it was not an anthropoid, it might be an omomyid prosimian and I later stressed¹⁰ again the hominoid similarity. (7) Finally, Szalay has lately argued¹ that *Amphipithecus* is an advanced lemuroid.

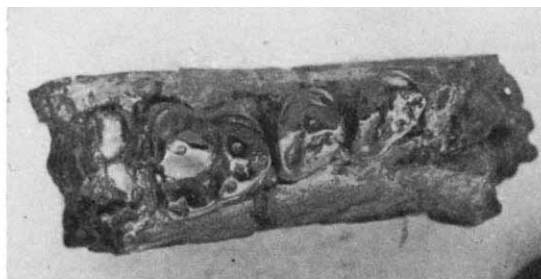
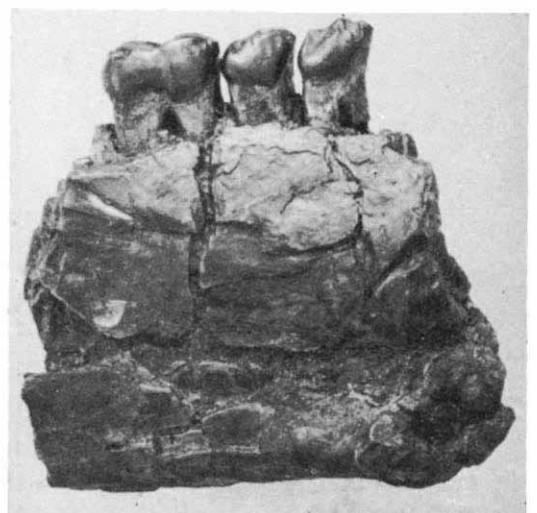
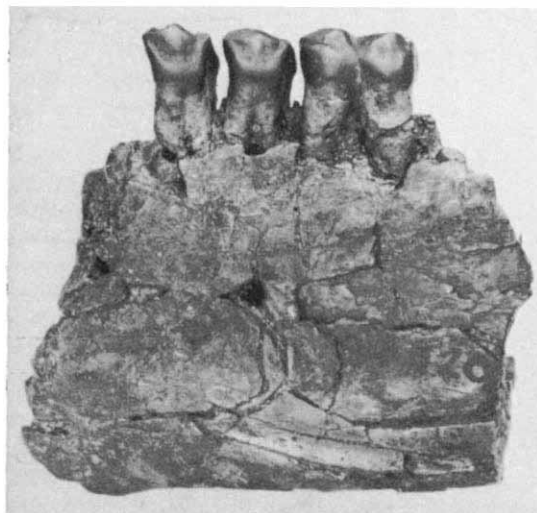


Fig. 1 Crown view (above) and lateral view of the teeth and jaw of *Amphipithecus mogaungensis* from Colbert 1935. The single known specimen is from the late Eocene of Burma.



A solution of the relationships of *Amphipithecus* can be presented in three stages. First, a basic structural and behavioural difference separates all Condylarthra from Primates and equally separates the latter from a large number of later orders presumed to have been derived from the condylarths. Two such orders are Artiodactyla and Perissodactyla but others include most, if not all, of the paenungulate orders. These, in the interpretation of Simpson¹¹, constitute the orders Pantodonta, Embrithopoda, Dinocerata, Hyracoidea, Sirenia, Pyrotheria and Proboscidea. All the species belonging to these orders are apparently hoofed herbivorous feeders, which cannot convey food to their mouths with their fore or hind limbs. They therefore either have trunks, as in the extant Proboscidea and the extinct Pyrotheria, or lengthened mandibular horizontal rami, usually with elongated diastemata between the cheek teeth and an anterior cropping mechanism which consists either of flared and procumbent incisors in both jaws or of a horny pad opposing the lower incisors. Generalized primates have cheek teeth which are like those of certain artiodactyls and condylarths, but because primates typically use their hands to feed, it is only in Primates and not in Condylarthra or Artiodactyla that the front teeth are not separated from the cheek teeth (the whole tooth row is crowded anteroposteriorly). For the same reason the anterior teeth of certain primates have become relatively small and vertically implanted as seems to be the case in *Amphipithecus*^{2,3}.

Second, *Amphipithecus* also has an extremely deep mandible compared with the crown height of the cheek teeth preserved; this depth is greater than in almost all mammals with teeth in the same size range, and exceeds even that of the early ape *Aegyptopithecus* (see Fig. 1). Such deep mandibles are characteristic only of certain primates; for example, *Gigantopithecus*¹², many colobines and some platyrrhine monkeys. Great mandibular depth correlates with symphyseal fusion. *Homo* and other hominids also show early symphyseal fusion with small, vertically implanted incisors and have a symphyseal cross-section the long axis of which is oriented almost at right angles to the long axis of the tooth row or horizontal ramus of the mandible. When food gathering shifts to hand or trunk then the importance of incisors in this function decreases. In the case of lemurs and lorises, lower canines and incisors (freed from their food gathering function) have become dental combs for grooming the fur. Elephants have lost opposing front teeth altogether, for food is conveyed to the mouth principally by the trunk. On the other hand, the prosimians generally have anteriorly shallow, separate jaw rami with an unfused anterior symphysis. The few prosimian species that do show symphyseal fusion include the large extinct Pleistocene lemurs of Madagascar, *Archaeolemur* and *Hadropithecus*. These lemurs have long been recognized as having independently converged toward Anthropoidea, and their evolution serves to support the points raised here, for their dental formulae as well as other features prove they cannot be catarrhines although they parallel them. The jaws of prosimians, living or fossil, are never particularly deep. The incisors of such prosimians as the lorises and lemurs project forward and there is little or no development of either the superior or the inferior transverse tori at the back of the symphysis connecting and buttressing the two halves of the lower jaw. This is because these latter structures apparently reach fullest development as they further reinforce the fused symphysis characteristic of higher Primates, including Catarrhini and Platyrrhini. Both these tori are quite large in *Amphipithecus* and it may be that part of the superior transverse torus actually passes the mid-line, which seems likely if, as in all other Tertiary Anthropoidea, the mandibular rami diverged posteriorly. This, together with marked toral development, gives two lines of evidence that there was symphyseal fusion. It should be stressed that there are no primates known below the grade of Anthropoidea (=higher primates), and indeed there are no other mammals which show vertically oriented symphyseal sections, comparatively deep mandibles, orthally directed, crowded, teeth and large tori.

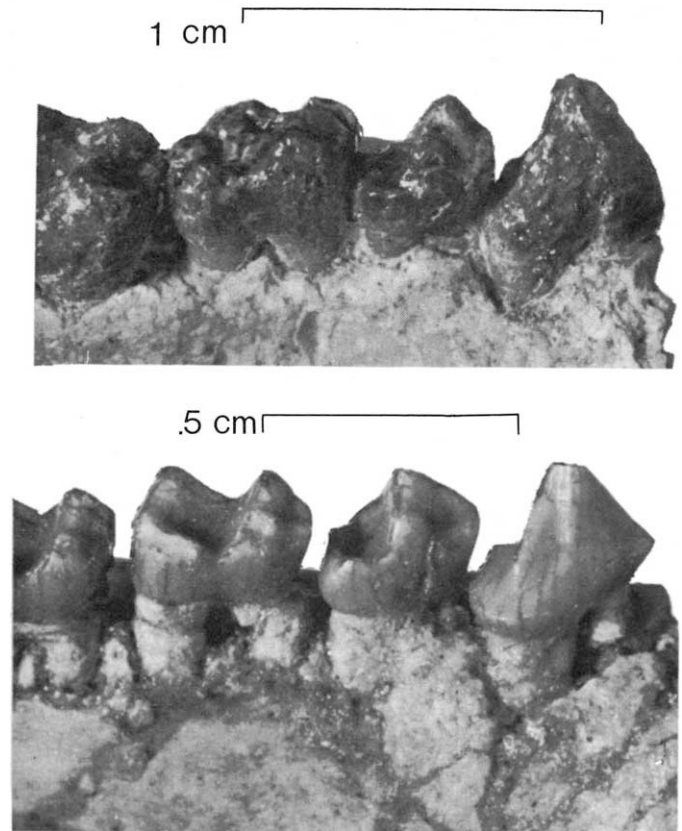


Fig. 2 Comparison of the internal aspect of the premolars and front molars of *Aegyptopithecus zeuxis* (above) and of *Oligopithecus savagei* (below). Both are from the Oligocene deposits of the Fayum badlands, Egypt.

Third, the objection that retention of three premolars is strange for a catarrhine primate has now lost any force it may have had because at least a dozen jaws of the undoubtedly early catarrhine primates *Apidium* and *Parapithecus* recovered recently by Yale University expeditions under my direction from the Oligocene Fayum of North Africa demonstrate that three premolars are consistently present. Both the Pondaung fauna as well as that of the Fayum contain species of the primitive anthracothere genus *Brachyodus*. This confirms a migration route of some sort between the two areas. Absence of M_1 hypoconulid, if it is indeed entirely absent in *Amphipithecus*^{1,2}, is not particularly strange, because this animal, even if a member of Anthropoidea, need not be ancestral to any later species retaining this structure. "Hypoconulids" can also arise as neomorphs. Modern cercopithecoids lack M_1 hypoconulids as do many early Primates. Moreover, the hypoconulid is not clearly distinct on M_1 in the archaic catarrhine *Oligopithecus*. This animal will be shown, in what follows, to be a higher primate. Further, Szalay (personal communication) now agrees that *Oligopithecus savagei* is not a prosimian but is a catarrhine.

If *Amphipithecus* is not a member of Anthropoidea then it will have to be considered as belonging to an order of mammals otherwise entirely unknown which might facetiously be called Pseudanthropoidea, or Pseudcatarrhini. *Oligopithecus* must be considered a catarrhine primate because of its complete similarity to Old World Anthropoidea: its jaw is deep, it has only two lower premolars and the anterior of these is elongate and serves as a hone against the back of the upper canine.

The P_2 or P_3 honing function of Anthropoidea is never seen in Prosimii and consequently the full development of this mechanism with highly heteromorphic P_3 and P_4 seen in *Aegyptopithecus* and *Oligopithecus* (Fig. 2) is additional evidence that these Fayum primates were definitely of a higher primate grade. Fig. 3 shows the honing facet of the unique

1 cm



Fig. 3 Stereopair of the anterior part of the left lower jaw of *Oligopithecus savagei* showing the distinct honing facet for the back of the upper canine—a distinctly anthropoid trait.

type mandible of *Oligopithecus savagei*. Clearly *Oligopithecus* is not a prosimian. Its premolars are fully heteromorphic and unlike anything that can be found in any prosimian, living or fossil. The tooth crown surfaces of the new *Aegyptopithecus* mandible have been chemically eroded but this has not obscured its premolar resemblance to *Oligopithecus*. In both P_3 's the trigonid is wide open lingually, and the paraconid ridge descends anteriorly just lateral to the mid-line in the long axis of the tooth row. The metaconid ridge of P_3 slopes posterolingually in both and ends in the same manner in a slightly enlarged bulb, the presumed homologue of the P_4 metaconid. In both there is an internal basal cingulum on P_3 but not on P_4 or on teeth posterior to it, and in both this cingulum carries a slight swelling just above the space between the large posterior and somewhat smaller anterior root of this tooth. In both species the entoconid and hypoconulid of M_2 are closely approximated. One difference (Fig. 2) is that the M_1 hypoconid of *Oligopithecus* is higher and less rounded than in *Aegyptopithecus*. The P_3 canine hone of *Oligopithecus* (Fig. 3) is well defined and the principal direction of the grinding stroke of the canine is indicated by striations on the wear facet. No prosimian, living or fossil, shows a premolar honing facet of this sort which does, of course, reflect that the functional uses of the front teeth of prosimians are basically different from this.

One or two observations about the unique type specimen of *Oligopithecus* seem worthwhile at this point. This specimen was found by D. E. Savage and was collected by me in December 1961 in quarry E of the lower fossil wood zone of the Jebel el Quatrani Formation, Fayum, Egypt. It was found in a porous lense of gravel-sized matrix. The body of the mandible had been considerably fractured with the result that its parts had expanded and the cracks had been refilled by sand grains. Thus, the teeth, once closed together from back to front, are now separated from each other by gaps. During collection the canine and P_3 were unavoidably further tilted apart (see Fig. 2). It has been considered inadvisable to try to move these teeth back into closer approximation because the horizontal body of the mandible is as soft and friable as chalk. As the teeth are now splayed apart, it might be thought that *Oligopithecus* had a P_2 , but when discovered in place there was no gap between these teeth, and the wear facet for the upper canine seen on P_3 (Fig. 3) completely confirms the lack of P_2 .

In sum, the overall structure of teeth and jaws of *Amphipithecus*, *Aegyptopithecus* and *Oligopithecus* shows numerous anatomical details which only resemble living catarrhine primates. These genera, together with *Proliopithecus*, *Aeolo-*

pithecus, *Apidium* and *Parapithecus*, are therefore the oldest undoubted evidence of Catarrhini. Although *Apidium* and *Parapithecus* of the Fayum do retain three premolars, the specifically catarrhine anatomy of the mandibles of *Oligopithecus* and *Aegyptopithecus* tends to weaken the conjecture that the Fayum primates might have been introduced to Africa by rafting across the South Atlantic Ocean from South America.

ELWYN L. SIMONS

Department of Geology and Geophysics,
Yale University,
New Haven, Connecticut 06520

Received January 19; revised April 9, 1971.

- ¹ Szalay, F. S., *Nature*, **227**, 355 (1970).
- ² Colbert, E. H., *Amer. Mus. Novit.*, No. 951 (1937).
- ³ Colbert, E. H., *Bull. Amer. Mus. Nat. Hist.*, **74**, Art. 6 (1938).
- ⁴ Piveteau, J., *Primates Paléontologie Humaine (Traité de Paléontologie)*, **8** (Masson, Paris, 1957).
- ⁵ Hürzeler, J., *Verh. Naturf. Ges. Basel*, **69** (1), 1 (1958).
- ⁶ Remane, A., in *Menschliche Abstammungslehre* (Fischer, Stuttgart, 1965).
- ⁷ von Koenigswald, G. H. R., *Proc. K. Ned. Akad. Wet.*, **68**, 165 (1965).
- ⁸ von Koenigswald, G. H. R., in *Neue Ergebnisse der Primatologie* (Fischer, Stuttgart, 1967).
- ⁹ Simons, E. L., in *International Encyclopedia of Social Sciences* (Macmillan, New York, 1968).
- ¹⁰ Simons, E. L., in *Problèmes Actuel de Paléontologie (Colloques Intern. Cent. Nat. Rech. Scient.)*, No. 163, 597 (1967).
- ¹¹ Simpson, G. G., *Bull. Amer. Mus. Nat. Hist.*, **85** (1945).
- ¹² Simons, E. L., and Ettel, P. C., *Sci. Amer.*, **222**, 76 (1970).

Selecting Tests in Diagnostic Keys with Unknown Responses

HERE we outline a method for constructing diagnostic keys from test results, some of which are unknown. The method is then modified to reduce the number of different tests used. Elsewhere¹ we discuss an application to yeasts, in which the primary purpose is not so much the construction of a key, but to find how few out of a set of tests is required to identify all the yeasts.

The average number (m) of steps required to identify a species can be calculated for any key. An obvious objective is to construct the key with smallest m . Other objectives include minimizing the average cost of identification and balancing

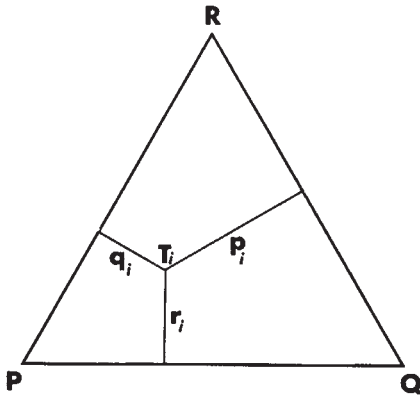


Fig. 1 Representation by areal coordinates of three proportions, $p_i(+)$, $q_i(-)$, and $r_i(?)$, for test T_i .

small m against the number of different tests used in the key. No algorithm seems to be known for minimizing m (apart from the impracticable one of enumerating all possible keys); but the empirical procedures discussed below give approximate solutions.

The results of the tests under discussion are usually presented in an all or none fashion (+ or -). The maximum number of species that can be separated by k binary tests is 2^k and, conversely, n species require at least $\log_2 n$ tests for complete separation. Tests that reduce the number of species to $< 2^k$ are not fully efficient². Hence, for any given set of species, in the best possible key (that with minimum m) every test divides its subjects into two groups of equal size. Because this arrangement is usually impracticable, an empirical method for constructing a key is to select tests that most nearly divide the species into equal groups. Several authors³⁻⁶ have discussed this approach to binary tests, but we also consider unknown responses, denoted by "?". These missing values may occur because a test result has not been observed, or is difficult to interpret, or, as in the example discussed by Barnett¹, the test results are variable so that their proper handling would require a probabilistic key, with the additional complications of considering probabilities of misidentification.

When constructing the key, any species with a ? response to a given test used for branching must be included in both + and - branches and hence may appear at a number of ends of the tree. When using the key, any ? response to a test must lead to both + and - branches, so that a specimen may be given several possible identities. At each dichotomy of the key, the test to be selected is that for which the number of + responses most nearly equals the number of - responses, allowing for the ? responses. The selection criterion must depend on the proportions p_i , q_i , and r_i of +, -, and ? responses. The i th test may be represented by a point $T_i(p_i, q_i, r_i)$ in three dimensional space, but because $p_i + q_i + r_i = 1$, all points T_i are inside (or on) the equilateral triangle PQR (Fig. 1) cut off by the coordinate axes on the plane $p + q + r = 1$. The perpendiculars

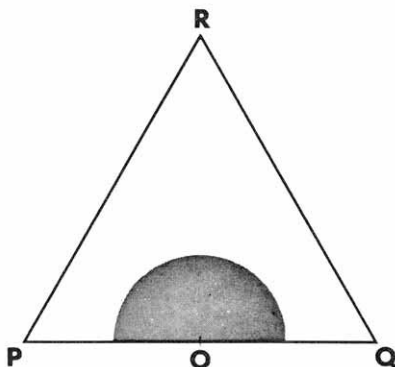


Fig. 2 All tests represented by points on a semicircle, centre O (mid-point of PQ), are equally efficient.

from T_i on to QR , PR and PQ have lengths $\sqrt{3}/2$ times p_i , q_i and r_i , respectively, and are usually termed areal coordinates. k tests can be represented as k points T_i ($i = 1, 2, \dots, k$) within the same triangle. If there are no ? responses, the point T_i lies on PQ and the selected test is that nearest O , the mid-point of PQ , that is the test for which $p_i = q_i = \frac{1}{2}$ is most nearly true. When there are ? responses, the most efficient test is here taken to be that for which OT_i is shortest, $OT_i^2 = (p_i - \frac{1}{2})^2 + (q_i - \frac{1}{2})^2 + r_i^2$. On this measure of efficiency, all those tests represented by points on any semicircle (centre O) and within triangle PQR are equally efficient; those within the semicircle are more efficient than those outside it (Fig. 2).

We considered other criteria of test efficiency; for example, the information criterion $I_i = (p_i + r_i) \log(p_i + r_i) + (q_i + r_i) \log(q_i + r_i)$ behaves almost identically to OT_i^2 , especially in the region containing efficient tests. The Williams and Lambert association analysis⁷ and its extension suggested by Gower⁸ have not yet been tried. The criterion of OT_i^2 was chosen for its simplicity, providing an efficient algorithm when included in a computer program; it can also be extended easily to cope with multilevel responses. These virtues are important for computing when the results of many tests have to be examined at every level of the hierarchic key under construction. When several tests are nearly equally efficient, the simplest procedure is to select any one at random, and in practice to select the first encountered.

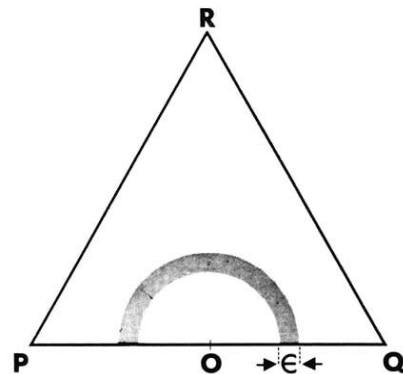


Fig. 3 To increase the chance of finding previously used tests, all points in the annulus, width ϵ , are taken to represent equally efficient tests.

In botanical identification a step by step method is often used; each test or observation is done consecutively, and the test use at any stage is determined by the outcome of the previous test. Keys constructed by the method described here should then be satisfactory. By contrast, in identifying micro-organisms it is usual to do many tests simultaneously before referring to a key. When many hundreds of organisms have to be identified in a year, it may be important to minimize the number of tests that have to be done. A further objective is to partition the key so that the results of the first set of tests determine which tests are in the second set; in this way the number of tests for identification may be greatly decreased.

To minimize the number of tests used, the criterion described was modified to increase the chance of finding a test that occurs elsewhere on a different branch of the key. This was done by regarding as equally efficient all tests within an annular region of width given by the difference between the radii OT and $OT + \epsilon$ (Fig. 3). Several values of ϵ (0, 0.05, 0.1, 0.3, 0.5) were tried for sixty-eight species of fruit yeasts; m ranged from 6.61–6.84, and the number of different tests from twenty-four to twenty-five. Here, at least, little was gained by varying ϵ . This was mainly because certain tests were essential for separating pairs of similar species; although these tests were not needed in the earlier levels of the key, they had to be included later. When selecting one of several tests in the ϵ -annulus, two

strategies were tried. The selected test was either (i) that used most often before, or if none, the most efficient test, or (ii) the most efficient test of those used before, irrespective of how often used.

To obtain partitioned keys with this program, a modification of the ϵ -process might be used, although it was not tried. In this method, the highest level of the key at which each test has been used is recorded, and the best test used previously at the highest level is selected from the ϵ -annulus. The computer program constructs the key by completing the branches from left to right. Alternatively, the levels from top to bottom could be completed; this would be more suitable when trying to minimize the number of tests used in different partitions of the key, but it is less efficient computationally. This strategy, and that of building the key from bottom to top, are being investigated.

Two or more tests used simultaneously may give more help in identification than both used separately; in this context Pankhurst⁴ has a simple but effective formula for + and - responses only. Following the success of applying the present work, as described in the companion paper¹, we are investigating the handling of ? responses when considering two or more tests simultaneously, and also studying the effects on the calculations of permuting the order of the tests.

J. C. GOWER

Rothamsted Experimental Station,
Harpenden, Hertfordshire

J. A. BARNETT

Food Research Institute,
Norwich NOR 70F

Received November 23, 1970; revised April 16, 1971.

¹ Barnett, J. A., *Nature New Biology* (in the press).

² Barnett, J. A., *Antonie van Leeuwenhoek*, **23**, 1 (1957).

³ Gower, J. C., in discussion on Marshal, A. W., and Olkin, I., *J. Roy. Statist. Soc., B*, **30**, 438 (1968).

⁴ Pankhurst, R. J., *Computer J.*, **13**, 145 (1970).

⁵ Pankhurst, R. J., *Nature*, **227**, 1269 (1970).

⁶ Hall, A. W., *Taxon*, **19**, 12 (1970).

⁷ Williams, W. T., and Lambert, J. M., *J. Ecol.*, **47**, 83 (1959).

⁸ Gower, J. C., *Biometrics*, **23**, 623 (1967).

Electron Microscope and Optical Diffraction Studies on Isolated Cell Walls from *Chlamydomonas*

THERE are few high resolution electron microscope studies specifically concerned with the architecture of the cell walls of the green alga *Chlamydomonas*. Sager and Palade¹ state that the wall of *C. reinhardtii* is a multilayered structure about 40.0 nm thick and that the structure is consistent with the cellulose wall described from light microscope observations. The description of the wall given by Walne^{2,3} and by Cavalier-Smith⁴ is essentially similar to that given by Sager and Palade. Barnett and Preston⁵ using the freeze etching technique reported the presence of oriented microfibrils in the cell walls. The regular features were interpreted as being cellulose which was thought to be synthesized by small granules associated with the surface of the plasmalemma. In the related species *C. moewusii* the wall had a regular periodicity of 23.3 nm, and again the striations were interpreted⁶ as being cellulose fibrils, but it was noted that the spacings were smaller than those observed in other structures containing cellulose fibrils⁷.

The preliminary findings we wish to report concern the application of various chemical and physical methods to the isolation and characterization of the cell wall material isolated from *C. reinhardtii* with particular reference to the ultrastructural features and their analysis by optical diffraction^{8,9}. In addition to the wild type strain we have examined two of a series of mutant forms we have isolated¹⁰, which show defects in various

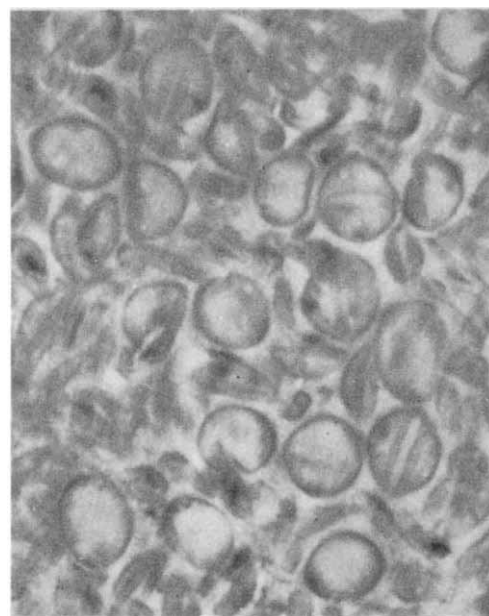


Fig. 1 Phase contrast micrograph of isolated cell wall fraction.

aspects of cell wall biogenesis. Cell preparations were obtained from liquid cultures and concentrated by low speed centrifugation. Pellets were placed in a Mickle shaker and disintegrated in the presence of glass beads. Fractions containing cell wall material were obtained by differential centrifugation as applied to the separation of bacterial cell walls¹¹. Centrifuged pellets containing walls were monitored for purity by examination in the phase contrast microscope and by electron microscopy. The purity and concentration of a typical cell wall fraction are illustrated in Fig. 1. Examination of shadowed specimens in the electron microscope revealed typical cell walls of the type shown in Fig. 2. The striations observed at low magnification were essentially similar to those reported by Lewin *et al.*⁶ but the spacing of 13.5 nm determined from Fourier transforms was considerably smaller (Fig. 2 inset).

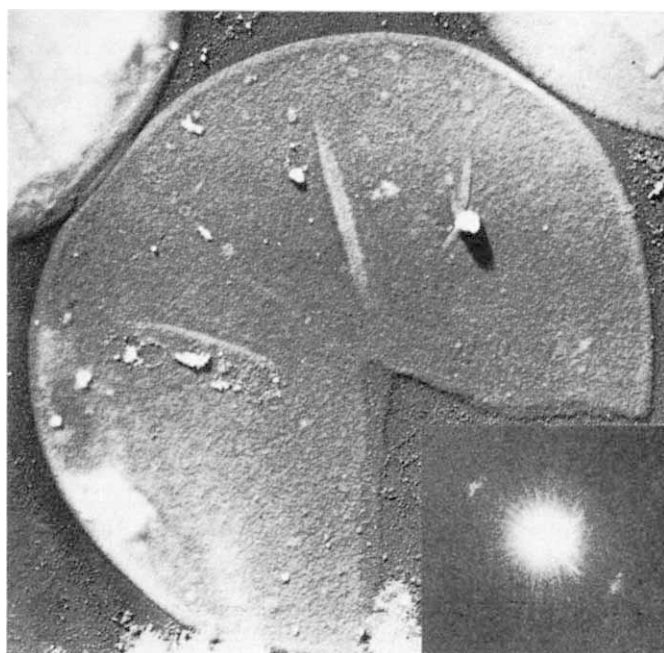


Fig. 2 Electron micrograph of shadowed cell wall. Inset: optical transform obtained from a shadowed cell wall, indicating regular periodicity of 13.5 nm.

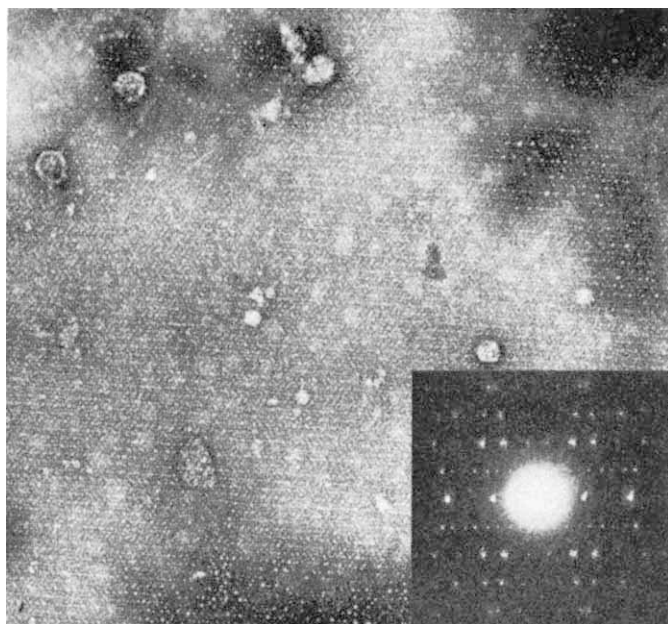


Fig. 3 Electron micrograph of negatively stained preparation of cell wall showing a regular lattice structure. Inset: optical transform from the same area.

Studies of thin sections of intact cells and cell wall fractions prepared by a variety of fixation and staining procedures showed the wall to have a structure similar to that described by the workers mentioned earlier. It was constructed of several electron dense layers arranged approximately parallel to each other. The layered region was about 19.0 nm across (after osmic glutaraldehyde fixation). In addition to the electron dense layered regions, the inner and outer surfaces of the cell wall when seen in thin sections showed different morphological features. At the inner surface a diffuse region was observed and appeared to consist of small particulate material, whereas the outer surface suggested the presence of long filamentous structures of about 3.4 nm in diameter being released from the wall.

After preparation of the wild type cell wall material in the presence of 2% ammonium molybdate or 2% potassium phosphotungstate (pH 6.8), and examination at high instrumental magnifications in the electron microscope, micrographs were recorded showing a well defined lattice pattern as illustrated in Fig. 3. Examinations of the micrographs in an optical diffractometer indicated that the cell wall was constructed of a complex lattice as shown in the inset of Fig. 3. The lattice structures appear to form layers in the cell wall and are positioned at preferred angles relative to each other. In the case of the pattern illustrated in Figs. 3 and 4, it is possible to interpret the structure as being two basic layers orientated at about 20°. The values relating to the layer lines from the crossed lattice are indicated in the diagram of Fig. 3 which is from the Fourier transform of the inset of Fig. 3. High resolution electron micrographs suggest that the diameter of the fibrils comprising the lattice determined from negatively stained specimens is about 3.8 nm (fifty measurements). The two mutants examined, CW2 and CW20, are defective in that the former cannot attach the wall to the plasma membrane and sheds it into the medium, and the latter, though having an attached wall, has no structural rigidity provided by its wall. Examination of the isolated walls from these mutants, however, revealed that the structural features and the spacings of the lattice were identical with those seen in the wild type wall.

Previous observations^{1,2} relating to the composition of *C. reinhardtii* have suggested that about 50% protein dry weight is present in the cell wall. Our own preliminary analysis of the

amino-acid composition of the isolated cell wall fraction points to a value of about 35% protein dry weight, but a more detailed analysis is in progress and will be reported later.

We have carried out a number of experiments on the treatment of isolated cell walls of *C. reinhardtii* with trypsin prepared according to the methods of Kosta and Carpenter¹³. Those treated with trypsin for 2 h at 37° C no longer retain the regular lattice structure as determined by electron microscopy. Following prolonged treatment with the enzyme they become disorganized and retain only a vague resemblance to their original shape and size. Treating the walls with 10 M KOH incubated for 2 h at 50° C also resulted in the loss of all morphological features corresponding to the original lattice and overall structure detectable by light and electron microscopy. Moreover, there was no evidence to show the presence of fibrils which would correspond to cellulose microfibrils in either the trypsin digests or after KOH extraction. In addition to treatment with trypsin and KOH extraction, several experiments were carried out in an attempt to remove the lattice structure with cellulases. Treatment with cellulase enzyme failed to remove or change the lattice material.

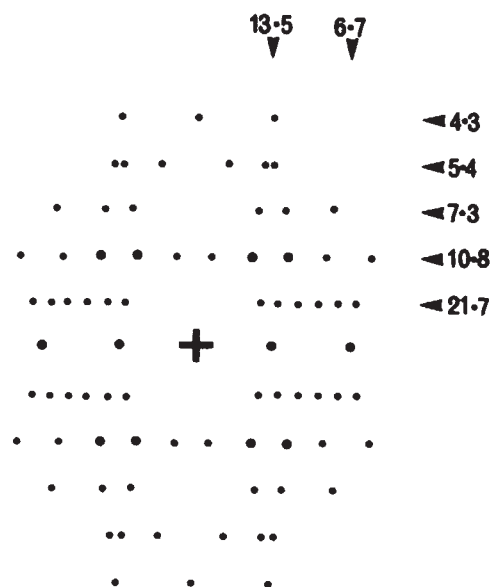


Fig. 4 Diagram of the lattice and layer line spacings in nanometres from the Fourier transform shown in the inset of Fig. 3.

The tacit assumption from earlier publications that the primary structural element of the cell wall of *Chlamydomonas* is composed of cellulose microfibrils gains no support from our observations. On the contrary our microscopical and chemical evidence indicates a structure in some ways analogous to that seen in certain bacteria¹⁴. The most pertinent question to be answered relates to the assembly mechanism which gives rise to the regular lattice structure depicted in Fig. 3, and in this context the eighty mutant forms we now have available which are defective in various aspects of cell wall biogenesis will be particularly useful. Our most recent studies suggest that the basic structural units for the wall are assembled from individual layers at the inner wall surface. This material, located between the plasmalemma and the cell wall, seems to be morphologically different from the slender strands which can be seen being released at the outer cell wall surface. Our tentative interpretation of these observations is that while assembly of units occurs at the inner wall surface, at the outer region of the cell wall, layers are being shed into the surrounding medium as long slender flexuous filaments with dimensions close to the structures forming the lattice pattern described above.

We thank Mr M. Rees for carrying out the preliminary

amino-acid analysis, Mr G. J. Hills for assistance in optical diffractometry, and Mr S. Frey for photographic assistance.

R. W. HORNE
D. R. DAVIES
K. NORTON
M. GURNEY-SMITH

John Innes Institute,
Colney Lane,
Norwich NOR 70F

Received January 15, 1971.

- ¹ Sager, R., and Palade, G. E., *J. Biophys. Biochem. Cytol.*, **3**, 463 (1957).
- ² Walne, P. L., *Amer. J. Bot.*, **53**, 908 (1966).
- ³ Walne, P. L., *Amer. J. Bot.*, **54**, 564 (1967).
- ⁴ Cavalier-Smith, T., thesis, Univ. London (1967).
- ⁵ Barnett, J. R., and Preston, R. D., *Proc. Roy. Microsc. Soc.*, **4**, 135 (1969).
- ⁶ Lewin, R. A., Owen, M. J., and Melnick, J. L., *Exp. Cell Res.*, **2**, 708 (1951).
- ⁷ Mühlethaler, K., *Biochim. Biophys. Acta*, **3**, 527 (1949).
- ⁸ Horne, R. W., and Davies, D. R., *Septième Congrès Intern. de Microscopie Électronique*, Grenoble, **3**, 117 (1970).
- ⁹ Klug, A., and De Rosier, D. J., *Nature*, **212**, 29 (1966).
- ¹⁰ Davies, D. R., and Plaskitt, A., *Genet. Res.*, **17**, 33 (1971).
- ¹¹ Salton, M. R. J., *The Bacterial Cell Wall*, 42 (Elsevier, Amsterdam, 1964).
- ¹² Gotelli, J. B., and Cleland, R., *Amer. J. Bot.*, **55**, 907 (1968).
- ¹³ Kosta, V., and Carpenter, F. H., *J. Biol. Chem.*, **239**, 1799 (1964).
- ¹⁴ Glauert, A. M., and Thornley, M. J., *Ann. Rev. Microbiol.*, **23**, 159 (1969).

Wolffia arrhiza as a Possible Source of Inexpensive Protein

THE development of new foods is vital to the needs of the rapidly expanding population in Asia. But apart from the necessity of being competitive in market price, they must be acceptable to the human palate, a requirement that has often frustrated attempts to introduce new foods. In this light, the improvement of production and processing of a commodity which is currently marketed for direct human consumption but on a small and inefficient scale has several advantages. Such a commodity is the aquatic plant, *Wolffia arrhiza* Wimm., Lemnaceae, known to have been used as a vegetable by the Burmese, Laotians and the people of northern Thailand for many generations. The local Thai name for the plant, "khainam", may be literally translated as eggs of the water and suggests the oval shape of the plant (length 1.5 mm, width 1.0 mm). Khai-nam is generally regarded as a poor people's food and has attracted little attention as a potentially significant source of human food. The species also occurs in India¹, but no report has been made pertaining to its application as a food source in that country.

We have observed the native methods of cultivating *Wolffia arrhiza* and have analysed samples. Small scale cultivation by rain-fed open ponding methods is carried out by villagers living near provincial urban centres in northern Thailand. The pH of the water in all the ponds visited (more than 100) was between 6.5 and 7.0, and most were small (60–100 m²) and shaded by bamboo groves. No chemical fertilizers or manures were added. In controlled laboratory conditions, *Wolffia* has been found to reproduce vegetatively by budding and to have a generation time of approximately 4 days^{2,3}. But natural conditions with higher light intensities and temperatures seem to be more conducive to growth. In practice, the plants are harvested at intervals of 3 to 4 days during which period the relatively small number of plants remaining from the previous harvest multiply into a thick mass of yellowish-green plants at the water's surface indicating that several generations may have arisen within 4 days. Longer time intervals between harvests invariably lead to lower yields and a product con-

taining a significant portion of dead brownish individual plants which, being unattractive, fetch a low market price. A record of harvesting over a period of 4 months from randomly chosen ponds revealed that the average yield of fresh marketable plants (collectively containing an average of 4% dry matter) is 0.68 kg/m²/week.

In the climatic conditions of the town of Chiangmai in northern Thailand (lat. 19° N, long. 99° E), *Wolffia arrhiza* remains in its edible vegetative form between November and July. The inedible sexually reproducing form prevails between August and October. On the basis of a 9 month period of productivity the calculated annual yield is 265 tons/ha fresh weight or 10.5 tons/ha dry weight. The chemical composition and annual areal yields of *Wolffia* are listed and compared with conventional crop yields in Table 1.

Table 1 Proximate Analysis and Yields of *Wolffia arrhiza* in Comparison with Conventional Crops

Component	<i>Wolffia</i> , dry weight %	Average yield (kg/ha/year)				
		<i>Wolffia</i>	Soybean	Ground-nut	Rice	Corn
Protein	19.8	2,080	303	229	71	179
Carbohydrate	43.6	4,589	255	164	849	1,451
Fats	5.0	533	158	397	4	87
Fibre	13.3	1,398	44	21	3	40
Ash	18.3	1,928	41	20	5	24
Water	0	0	89	51	124	238
Total	100.0	10,528	890	882	932	1,772

The protein nitrogen was determined by the Kjeldahl method. Fats were extracted by the Soxhlet technique using dichloromethane. The rice was converted from paddy to dehusked rice (ratio 0.66) and groundnut was converted from unshelled to shelled groundnut (ratio 0.60). We determined the composition of *Wolffia*; those of crops were computed from US Department of Agriculture data⁴. Other data on conventional crops were obtained from the Food and Agriculture Organization⁵.

In terms of annual yield, *Wolffia* produces more dry matter than the traditional crops grown in Thailand. The protein yield of *Wolffia* is several times greater than those of the local crops. So far, no attempts have been made to increase yields by improving growth conditions but studies will be undertaken to determine the effects of supplemental nutrients, controlled incident solar radiation, harvesting periodicity and mixing in batch and continuous outdoor conditions. Dependent variables will include growth rates, areal yields, proximate analyses of the product, water requirements, nutritional value, production economics and market potential. The research will be directed towards establishing optimum production conditions giving greater yields at lower costs. The naturally occurring species, *Wolffia arrhiza*, will be studied first because of its proven market and nutritional acceptability.

KRACHANG BHANTHUMNAVIN

Department of Biology,
Faculty of Science,
Mahidol University,
Bangkok 4, Thailand

MICHAEL G. MCGARRY

Division of Environmental Engineering,
Asian Institute of Technology,
Bangkok 5, Thailand

Received March 12; revised April 29, 1971.

¹ Fischer, C. E. C., in *Flora of the Presidency of Madras*, Part IX (edit. by Gamble, J. S.) (Adlard and Son, London, 1931).

² Sakdisuwan, S., thesis, Chulalongkorn Univ., Bangkok (1967).

³ Vacharabhaya, M., thesis, Chulalongkorn Univ., Bangkok (1969).

⁴ *Composition of Foods, Agricultural Handbook No. 8* (United States Department of Agriculture, Agricultural Research Service, Washington, 1963).

⁵ *Production Yearbook*, **23** (Food and Agriculture Organization, Rome, 1969).

Effect of Purified Luteinizing Hormone Releasing Factor on Normal and Hypogonadotrophic Anosmic Men

THE occurrence of familial and nonfamilial cases of hypogonadotrophic hypogonadism and hyposmia or anosmia (Kallman's syndrome) has been well documented^{1,2}. Because the disease has been found only in humans, little is known about the site of the gonadotrophic lesion. Pathological examination of the pituitary glands of these patients has not

(1.6 ± 0.1 mIU/ml. (F. G.); 1.8 ± 0.15 mIU/ml. (G. G.)) to peaks at 2.7 and 3.5 mIU/ml. respectively 10 min after infusion began. Although the responses were small, they are within the sensitivity of the method and we believe that they represent a real response. At no time during the preceding 6 months did repeated control levels of plasma LH exceed 2.0 mIU/ml. in the two experimental subjects or in two other affected members of this kinship who had not received testosterone. There was no immunological LH activity in the LRF preparation when it was tested in assays which measure sheep or human LH. The possibility of a non-specific response is

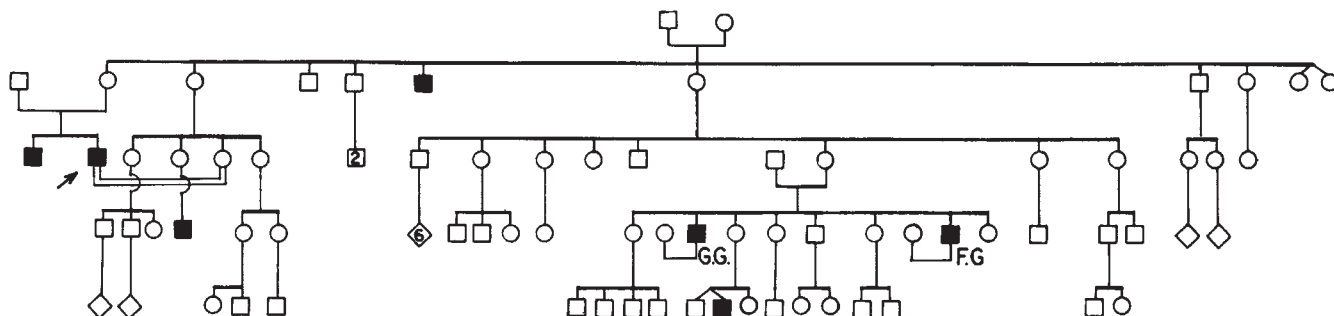


Fig. 1 Pedigree of the hypogonadotrophic subjects. Closed squares denote males with hypogonadotrophic hypogonadism and anosmia.

revealed any abnormality³. No estimates of pituitary gonadotrophin content in patients with hypogonadotrophic hypogonadism are available, although patients who have normal amounts of circulating follicle stimulating hormone but who lack luteinizing hormone (LH)—the so-called "fertile eunuch syndrome"—have been described. In contradistinction to the Kallman syndrome, these (potentially) fertile patients have a normal sense of smell and testicular development with varying degrees of spermatogenesis⁴. Injections of gonadotrophic substances cause an appropriate gonadal response in patients with Kallman's syndrome⁵ and the lesion is considered to be central in origin⁶. Attempts to stimulate the release of gonadotrophin in these patients by the use of the antioestrogen clomiphene citrate have been unsuccessful⁷.

We have used purified luteinizing hormone releasing factor (LRF) to study these individuals. Two brothers aged 28 and 30 with hypogonadotrophic hypogonadism and anosmia are part of a kinship demonstrating this syndrome (Fig. 1). F. G. (age 28) had taken methyl testosterone (25 mg twice a day) with both subjective and objective signs of androgenization until 2 weeks before receiving LRF. G. G. (age 30) had taken 10 mg of methyl testosterone daily without any response. G. G. was pretreated with clomiphene citrate (300 mg daily for 5 days followed by 5 days of no treatment) before receiving LRF. Both patients were given 300 median eminence extract equivalents (MEE) of purified ovine LRF in physiological saline solution (stage three⁸ prepared by Dr H. Gregory) by intravenous drip over a period of 3 and 6 min respectively without untoward effects after an initial episode of flushing. A normal male control (M. B., age 32) was given 100 MEE of ovine LRF by intravenous drip over a period of 7 min. All three subjects had an intravenous physiological saline drip running for 30 min before injection of LRF. The subjects were unaware of the time that the LRF infusion began. The results of this treatment were measured by radioimmunoassay of plasma LH⁹ and are shown in Fig. 2. As expected, in the control male there was an abrupt increase in plasma LH with a characteristic time course including a peak 35 min after infusion began. The two hypogonadotrophic brothers had very low levels of plasma LH which at no time during treatment reached the lower limits of normal for males although they had received an LRF dose three times that given the normal male. Yet both had a rise of plasma LH from control values

ruled out by the lack of response to the control infusion and the characteristic timing of the responses to the LRF infusion¹⁰. The lack of an effect of stress on LH levels in the male has been reported⁹. All three subjects showed what may have been a slight secondary peak in plasma LH 2 h after infusion with LRF. Dosing with clomiphene citrate (300 mg/day) did not have a measurable effect on plasma LH in subject G. G. Nor can we see any potentiating or other effect of the clomiphene pretreatment of the response of G. G. compared with F. G.

The minimal responses in affected patients could reflect a lesion in the pituitary gland or be the result of chronic depriva-

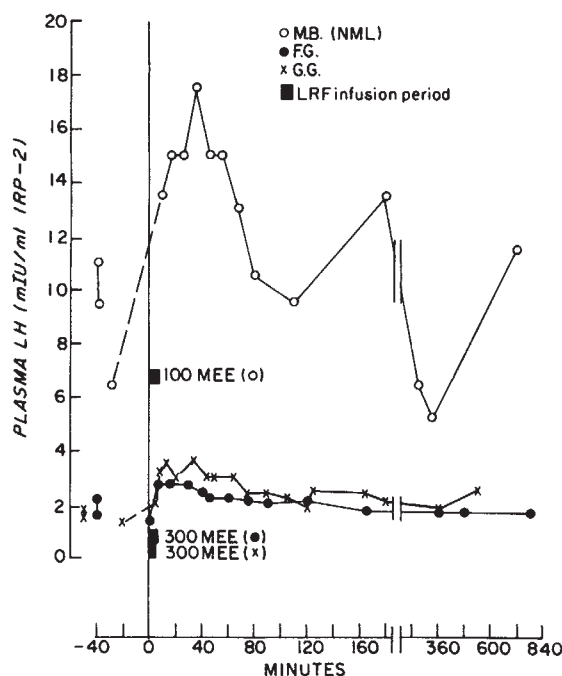


Fig. 2 Plasma LH during control periods and after LRF infusion. O, M. B. (NML); ●, F. G.; ×, G. G.; ■, LRF infusion period.

tion of releasing factors secondary to a central nervous system disorder. In this regard studies utilizing more prolonged dosage or measurement of pituitary gonadotrophic content in these patients will be of interest.

We thank Dr C. Alvin Paulsen for reagents and Mr M. C. Sood for technical assistance. Part of this work was supported by a grant from the Medical Research Council and a special research fellowship, National Institute of Child Health and Human Development, US Public Health Service (to F. N.).

F. NAFTOLIN*
G. W. HARRIS

MRC Neuroendocrinology Unit,
Department of Human Anatomy,
University of Oxford

M. BOBROW

MRC Population Genetics Unit,
Headington, Oxford

Received May 5, 1971.

* Present address: Department of Obstetrics and Gynecology, School of Medicine, University of California, San Diego, PO Box 109, La Jolla, California 92037.

- ¹ Kallman, F., Schonfeld, W. A., and Barrera, S. E., *Amer. J. Ment. Defic.*, **48**, 203 (1944).
- ² Nowakowski, H., and Lenz, W., *Recent Prog. Hormone Res.*, **17**, 53 (1961).
- ³ Gautier, G., *Acta Neuroveg.*, **21**, 345 (1960).
- ⁴ Faiman, C., Hoffman, D. L., Ryan, R. J., and Albert, A., *Mayo Clin. Proc.*, **46**, 661 (1968).
- ⁵ Paulsen, C. A., in *Textbook of Endocrinology*, fourth ed. (edit. by Williams, R. H.), 405 (Saunders, Philadelphia, 1968).
- ⁶ Bardin, C. W., Ross, G. T., Rifkind, A. B., Cargille, C. M., and Lipsett, M. B., *J. Clin. Invest.*, **48**, 2046 (1969).
- ⁷ Bardin, C. W., Ross, G. T., and Lipsett, M. B., *J. Clin. Endocrinol.*, **27**, 1558 (1967).
- ⁸ Gregory, H., Walpole, A. L., Charlton, H. M., Harris, G. W., and Reed, M., in *Pharmacology of Hormonal Polypeptides and Proteins* (edit. by Martini, L., and Paoletti, R.), 123 (Plenum Press, New York, 1968).
- ⁹ Naftolin, F., Espeland, D., Tremann, J. A., Dillard, E. A., and Paulsen, C. A., in *Gonadotropins* (edit. by Rosenberg, E.), 373 (Geron-X, Los Altos, California, 1968).
- ¹⁰ Bayman, I. W., Harris, G. W., and Naftolin, F., *J. Physiol.*, **210**, 3P (1970).

Haemoglobin Type and Fertility of Merino Ewes grazing Oestrogenic (Yarloop Clover) Pastures

CLOVER infertility disease in sheep is attributed to the high concentrations of oestrogenic substances found in certain legumes such as subterranean clover, variety Yarloop¹. Reduction in flock fertility can be as high as 75% with additional losses of lambing ewes due to dystocia^{2,3}. Where large areas of these clovers are grown, as in western and southern Australia, the economic loss is considerable. Significant progress has been made in selecting clover varieties which have a low oestrogen content⁴ but replacement of established oestrogenic species has had limited success and the cost of renovation is often prohibitively high. We wish to report some observations which suggest that it may be possible to select and breed animals likely to be resistant to clover infertility disease using existing flocks classified on the basis of their haemoglobin (Hb) type.

The reproductive performance of fifty South Australian Merino ewes (Koonoona strain) grazing Yarloop dominant pastures was compared with that of fifty similar ewes grazing neighbouring rye grass pastures essentially free of Yarloop clover. Both groups were mated for the first time at 1.5 yr of age in February 1969 and again in February 1970. Mating

and lambing performance was recorded and surviving ewes were Hb typed⁵ in November 1970.

The data from 1969 and 1970 showed similar trends and are presented as combined totals in Table 1. The small number of HbAA type ewes were combined with the HbAB types to allow statistical comparison (χ^2) of fertility between Hb types within pasture types. Fertility of ewes grazing Yarloop (53.0%) was significantly ($P < 0.001$) lower than that of ewes on grass pasture (83.1%). But on the Yarloop pasture, the HbBB types were significantly ($P < 0.01$) less fertile than HbAA + AB types suggesting that the HbA gene is associated with a fertility advantage on oestrogenic pastures which is not apparent on non-oestrogenic pastures.

Table 1 Fertility and Haemoglobin Type of Ewes grazing Yarloop versus Grass Pastures for 1969 and 1970

	AA	AB	BB	Total	χ^2 value of difference between Hb types (AA + AB) - (BB)
Yarloop pasture					
No. of ewes mated 1969	4	23	17		
1970	4	22	13		
Total	8	45	30	83	
No. of fertile matings	8	26	10	44	
% of fertile matings	100.0	57.8	33.3	53.0	7.55†
Grass pasture					
No. of ewes mated 1969	6	20	21		
1970	4	17	21		
Total	10	37	42	89	
No. of fertile matings	10	30	34	74	
% of fertile matings	100.0	81.1	80.9	83.1	0.32 (n.s.)
χ^2 values of fertility difference between pastures within Hb types	5.22*		15.35‡	18.17‡	

n.s., $P > 0.05$; * $P < 0.05$; † $P < 0.01$; ‡ $P < 0.001$.

The possibility of an association between Hb type and reproductive performance in sheep was first reported by Evans and Turner⁶, who investigated Peppin Merino flocks in the Cunnamulla district and Deniliquin district of eastern Australia and found that ewes with Hb type BB and HbAB were slightly more fertile than HbAA ewes. In contrast, Obst^{7,8} has found in experiments at Parndana Research Station, Kangaroo Island, using south Australian Merino (Bungaree strain) sheep that the HbAA ewes produced more lambs and that these lambs survived better than lambs from ewes of the HbAB or HbBB type.

In the light of this evidence, differences between the reports could be resolved by taking into account the previously unsuspected susceptibility of HbBB ewes to clover disease. Clover disease is a continuing problem on Kangaroo Island and it is therefore significant that Obst and Evans⁸ reported that the superior reproductive performance of the HbAA ewes was best expressed during wet lambing seasons when Yarloop clover tends to dominate in mixed pastures at Parndana. The nature of the relationship between Hb type and resistance or susceptibility to clover disease remains to be determined. Some ewes are resistant to clover disease, for even in severe outbreaks they maintain good reproductive performance in spite of the measured high oestrogen content of the pasture⁹.

It has been suggested that the oestrogenic activity of the plant isoflavones is due to their metabolic derivatives^{10,11} and individual differences in these transformations might be expected. Differences could exist in the ability of individual

animals to metabolize and excrete active substances. Alternatively, the Hb type itself may confer some yet unknown physiological advantage. HbA is known, for example, to have a greater affinity for oxygen than HbB with a different oxygen dissociation curve¹². Conceivably, this may have implications for gamete, embryo or foetal survival.

Haemoglobin type in sheep is controlled by a pair of alleles at a single locus⁵ and therefore the HbAA gene frequency of any flock can be readily increased by mating with HbAA type rams. If the relationship of Hb type to clover disease susceptibility is confirmed in Merino and other breeds by more extensive trials, now in progress, Hb type selection could provide a practical basis for low cost management of this disease.

J. M. OBST
R. F. SEAMARK

Department of Animal Physiology and
Department of Obstetrics and Gynaecology,
University of Adelaide

C. J. MCGOWAN

Department of Agriculture,
Parndana, Kangaroo Island,
South Australia

Received March 10; revised May 10, 1971.

- ¹ Moule, G. R., Braden, A. W. H., and Lamond, D. R., *Anim. Breed. Abst.*, **31**, 139 (1963).
- ² Bennetts, H. W., Underwood, E. J., and Shier, F. L., *Austral. Vet. J.*, **22**, 2 (1946).
- ³ Maxwell, J. A. L., *Austral. Vet. J.*, **46**, 533 (1970).
- ⁴ Gladstones, J. S., *Austral. J. Agric. Res.*, **18**, 713 (1967).
- ⁵ Evans, J. V., King, J. W. B., Cohen, B. L., Harris, H., and Warren, F. L., *Nature*, **178**, 849 (1956).
- ⁶ Evans, J. V., and Turner, H. N., *Nature*, **207**, 1396 (1965).
- ⁷ Obst, J. M., thesis, Univ. New England, Armidale, Australia (1968).
- ⁸ Obst, J. M., and Evans, J. V., *Proc. Austral. Soc. Anim. Prod.*, **8**, 149 (1970).
- ⁹ Beck, A. B., *Austral. J. Agric. Res.*, **15**, 223 (1964).
- ¹⁰ Braden, A. W. H., Hart, N. K., and Lamberton, J. A., *Austral. J. Agric. Res.*, **18**, 335 (1967).
- ¹¹ Shutt, D. A., and Braden, A. W. H., *Austral. J. Agric. Res.*, **19**, 545 (1968).
- ¹² Dawson, T. J., and Evans, J. V., *Amer. J. Physiol.*, **209**, 593 (1965).

Effects of Δ^1 -Tetrahydrocannabinol on Temporally Spaced Responding and Discriminated Sidman Avoidance Behaviour in Rats

SEVERAL investigators have attempted to find a safe but reliable means of determining whether a new drug will produce hallucinations in man¹⁻⁴. Smythies *et al.* have found that rats show a characteristic "hallucinogenic profile" on various standard behavioural tasks. We ran rats on two of these tasks—responding on a differential reinforcement of low rate (DRL) schedule and discriminated Sidman avoidance—after administration of Δ^1 -tetrahydrocannabinol (THC), a known hallucinogen for man⁵⁻⁷. We hoped to find out whether the rats would display the hallucinogenic behavioural profile; and by using the same dose range for each task, to find the dose-effect relationship.

The THC came from a single sample and was stored dry in a sealed container under nitrogen. Analysis by gas liquid chromatography (3% OV-17 on Gas Chrom Q, glass column 5 × 1/8 feet at 250°C) yielded 95% pure THC after 1 year of storage. The vehicle consisted of 50 μ l. of double-distilled

ethanol plus 950 μ l. of 1% 'Tween 80' in steroid suspending medium. The THC was added to the vehicle immediately before use.

A rat on a DRL schedule receives reinforcement (usually food or water) only if it pauses for a predetermined length of time (say 10 s) since its last response. Responses which occur before the end of the interval reinstate the entire interval and postpone reinforcement, so that the schedule promotes long interresponse times. Smythies *et al.*^{4,8} have reported that when rats have been trained on DRL 15 (s) their lever-pressing behaviour is susceptible to disruption by the administration of hallucinogenic drugs. Specifically, a relatively small dose of mescaline HCl (12.5 mg/kg) has "... an all or none inhibitory effect on positively reinforced behaviour. At the onset of action the animal stops pressing the lever quite suddenly and restarts abruptly sometime later"⁴. To the best of our knowledge, there have been no reports of other drugs producing this particular pattern of behaviour. Sample cumulative records obtained from our rats under 12.5 mg/kg mescaline on DRL 10 are shown in Fig. 1, and agree with those of Smythies *et al.* in spite of minor differences in procedure. The cumulative records clearly show a cycle of normal responding, complete cessation, and sudden return to accurate temporal responding. Our object was to find out if THC would produce the typical hallucinogenic (mescaline) profile.

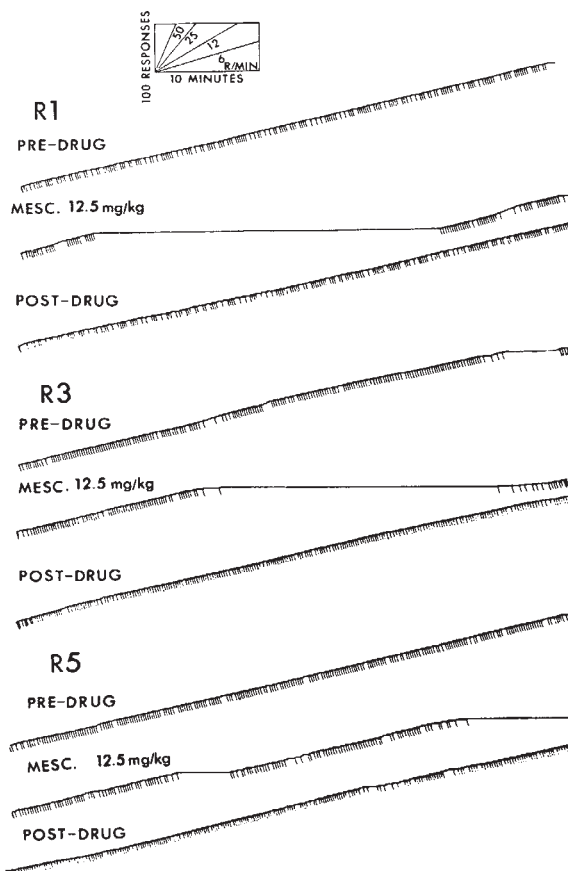


Fig. 1 Cumulative response records obtained from rats R1, R3, and R5 under 12.5 mg/kg of mescaline. Slope of line is a direct function of rate of responding. Reinforcements are indicated by downward pips. Records obtained on the day before drug (pre-drug) and the day following drug (post-drug) appear above and below the drug day.

Seven male hooded rats, about 200 days old at the beginning of the experiment, were maintained at 80% of their free-feeding body weight. A standard two-bar Grason-Stadler operant conditioning chamber with one bar removed served as the apparatus. Reinforcement consisted of 45 mg Noyes food pellets.

The principal experiment lasted 8 weeks. Animals were run daily for 60 min, 5 days a week. The DRL 10 schedule was in effect throughout. Week 1 was used to collect baseline data (that is, no vehicle or drug); during week 2 vehicle-only injections were administered on the second, third and fourth days of the 5-day week; and weeks 3–8 were drug weeks. On drug weeks each of six rats received one of six doses, each in a different order (latin-square design). The seventh animal also received all six doses and was run as a spare. During drug weeks, the appropriate dose of THC was injected on the third day of the week with the vehicle being injected on the second (pre-drug) and fourth (post-drug) days. Sessions began immediately after injection. Doses were: 1.5, 3.0, 4.5, 6.0, 7.5 and 9.0 mg/kg intraperitoneally. Total volume of each injection was 1 ml. An additional 6.0 mg/kg dose was administered to all subjects during the week after the completion of the latin-square.

Because the results were extremely variable, all the cumulative records were rated qualitatively according to the following scheme: (M)—mescaline-like (Smythies's DRL hallucinogenic profile: that is, more or less normal rate of responding with one or more fairly long pauses between runs of responding); (A)—amphetamine-like (substantial rise in response rate with decrease in reinforcements); (B)—below baseline rate (decreased responding, but sustained throughout the session); (C)—cessation (complete cessation of responding or cessation for more than half the session); (N)—no appreciable change from pre and post-drug days. The reliability of our classifications was checked by an independent rater not involved in the experiment. Only two of forty-nine total ratings were found to be discrepant. Not only was there wide variation in the quantitative effect at each dose, but the pattern of responding, as explained later, varied markedly from one drug test to another.

Examples of response patterns taken from various rats given different doses during this experiment are shown in Fig. 2. The important point is that, although behaviour was disrupted in twenty-two of the forty-nine cases, the Smythies's hallucinogenic profile was evident in only four records (one rat at 3.0 mg/kg, another at 4.5 mg/kg and another at both 6.0 and 9.0 mg/kg). Even with these four records the correspondence with Smythies's data was not impressive: response rate between pauses was increased as shown in R3's drug record (Fig. 2). Of the remaining eighteen records in which disruption was apparent, two were classified as Bs, two as As and fourteen as Cs.

It might be argued that the 1.5 to 9.0 mg/kg dose range used in the present study was simply too narrow, and that we might have produced more of the so-called hallucinogenic profiles had we used a different range. This does not seem likely in view of the fact that one of the four most mescaline-like profiles was obtained with a dose of 3.0 mg/kg and another was found at 4.5 mg/kg. Also, some behavioural change was evident during many of the THC test sessions. In a preliminary study we found that doses of 12.0 mg/kg produced complete cessation of bar pressing on a variable interval schedule; in this study there was a tendency for overall level of responding to decrease with increase in size of dose.

To find the effect of the drug on total response rate, an analysis of variance was performed on the ratio of the total drug-day responses over the sum of the drug-day responses and the pre-drug-day responses. A score of 0.5 would indicate no effect of the drug; a larger score, that the drug increased the response rate; a smaller one, that it decreased response rate. Mean ratio scores in order of increasing dose from the six rats in the latin-square were 0.44, 0.41, 0.40, 0.50, 0.31 and 0.25. The second 6.0 mg/kg dose yielded a mean score of 0.49. Ratios based on post-drug-day scores were similar, indicating that there were no drug carryover effects. A latin-square analysis based on the response ratio scores yielded dose ($F=2.34$, d.f.=5, 20) and animal ($F=2.40$, d.f.=5, 20) effects approaching statistical significance (in each case, $0.05 < P < 0.10$). The fairly high F value across animals

is probably because two rats were relatively unaffected by the drug. The drug effect can apparently be attributed to decreased performance at the two highest doses, an effect also found with the spare animal. There was no suggestion of a reliable effect across time ($F=0.74$), so an analysis of variance was completed with the ratio data from all seven rats. Mean ratio scores in order of increasing dose were 0.44, 0.42, 0.42, 0.51, 0.27 and 0.23. (The second 6.0 mg/kg dose yielded a score of 0.50.) The analysis revealed a significant dose effect ($F=3.93$, d.f.=5, 20, $P<0.01$). Analysis of the linear and quadratic trends showed reliable effects ($P<0.005$, $P<0.05$, respectively) but these effects together accounted for only 73% of the variance. The high performance at 6.0 mg/kg probably accounts for the rest.

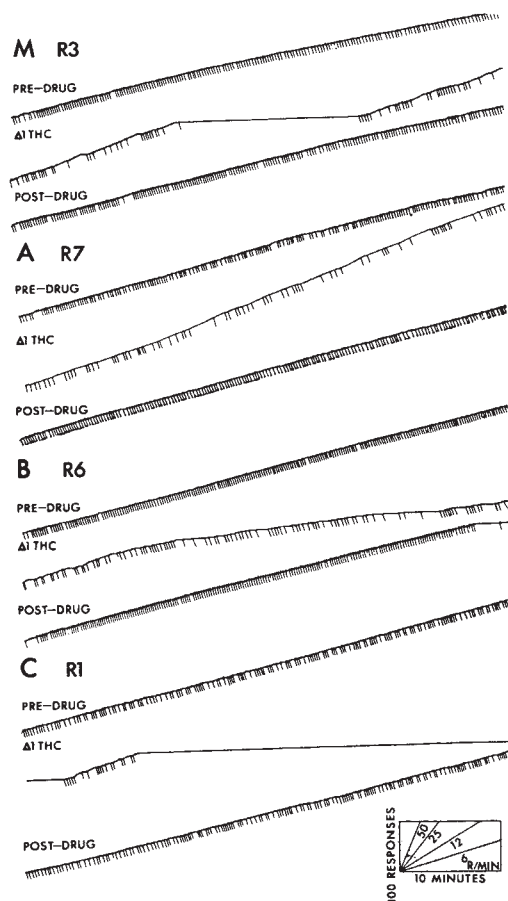


Fig. 2 Sample cumulative records portraying various response patterns under THC. Doses were 3.0, 6.0, 7.5 and 3.0 mg/kg for R3, R7, R6 and R1 respectively. See text for explanation of labels M, A, B, and C.

We decided to see if we could produce hallucinogenic profiles with mescaline. Accordingly, 2 weeks after the end of the principal experiment, all seven rats were given three 12.5 mg/kg intraperitoneal injections of mescaline spaced one week apart. The procedural details were identical to those already described except that saline was the vehicle. In sixteen of the twenty-one possible cases we produced Smythies-type profiles (Fig. 1).

Three weeks after the mescaline experiment, we administered a single 1.0 mg/kg intraperitoneal dose of α -amphetamine to five subjects. Except for one which did not respond at all, all rats had shorter IRTs⁹—the classic amphetamine effect on temporal discrimination.

The second procedure used was discriminated Sidman avoidance^{10,11}. This schedule is described by referring to three time intervals. If the subject fails to respond in the

response-signal interval a warning signal comes into effect and this marks the start of the signal-shock interval. If the animal fails to respond in the signal-shock interval a shock pulse is delivered at the end of that interval and the subject enters the shock-shock interval. During the shock-shock interval the signal remains on and shocks recur regularly. A response in the shock-shock interval terminates the signal and the response-signal interval is reinstated. All responses reinstate the response-signal interval to zero. Thus an animal may postpone signal onset by responding during the response-signal interval (premature responding); it may respond during the signal-shock interval (efficient responding) or, finally, it may respond in the shock-shock interval (late responding). After extensive training on this schedule, a subject concentrates its responses in the interval between signal onset and shock onset (efficient responding). The rat rarely delays pressing the bar until after shock onset (late responding) and only infrequently does it press before signal onset even though such responses are functional in postponing the onset of the signal and shock (premature responding). This discrimination can be disrupted by certain drugs: amphetamine increases premature responding and decreases late responding¹¹; chlorpromazine increases late responding and decreases premature pressing¹¹; and, according to Smythies *et al.*¹², hallucinogens such as mescaline, LSD-25 and N,N-dimethyl-tryptamine increase both premature and late responding.

The subjects were seventeen hooded male rats about 200 days old maintained at 300 g with water *ad libitum*. Twelve rats served in the actual experiment, five were pre-designated as spares on the basis of their relatively poor (below 85%) discriminated avoidance performance before the start of the experiment. The apparatus consisted of three small operant-conditioning chambers each equipped with a lever, loud-speaker and white light bulb. A clicker together with the light was the signal. Scrambled shock could be delivered to the grid floor of the chamber from a Grason-Stadler shock generator set at an intensity of 1.0 mA. Shock pulse duration was 0.5 s. Response-signal, signal-shock and shock-shock intervals were set at 32, 8 and 4 s respectively.

All seventeen rats had received 130 h of training before the experiment and were avoiding more than 75% of the shocks. During the study each rat was run for two 5-day weeks with a 9-day rest between each experimental week. Half of the rats were run on weeks 1 and 3, half on weeks 2 and 4. The following routine was observed during the experimental weeks; rats were given a 30 min "warm-up" period on each day after which they were removed from the apparatus, and either handled or injected and then returned to the operant chamber. The duration of each session was 165 min, excluding the warm-up period. On day 1 of each experimental week the animals were handled, on day 2 they were injected with vehicle, on day 3 they were injected with vehicle or vehicle plus drug, on day 4 they were injected with vehicle, on day 5 they were handled. Doses of THC were 0.75, 1.5, 3.0, 4.5, 6.0 and 9.0 mg/kg THC. Two subjects were tested at each level. One of the spare rats received 0.75, two 4.5 and two 9.0 mg/kg.

There was a significant decrease in discriminated avoidance performance when drug day scores were compared with pre-drug ($t=2.66$, d.f.=11, $P<0.05$) and with post-drug ($t=3.32$, d.f.=11, $P<0.01$) scores. There were no significant vehicle effects.

Modified Bovet-Gatti profiles for the twelve rats in the experiment proper are shown in Fig. 3. In the majority of cases the profiles conform to those reported for other hallucinogens¹², that is, an increase in both premature and late responding, with a resulting decrease in efficient responses. Similar data were obtained from the spare rats. Examination of cumulative response records showed that, judging from the number of shocks received early in the session, onset of drug action was rapid. As the session progressed, premature responding increased and the subjects often failed to press

in the presence of the signal. In most cases these effects persisted throughout the fairly long (165 min) session.

The THC effect was produced in both subjects tested with 1.5 mg/kg. This result, which we have repeatedly confirmed in subsequent experiments, shows that the discriminated Sidman avoidance schedule is sensitive to relatively low doses of THC. Even at 0.75 mg/kg the behaviour was disrupted in one of the two subjects.

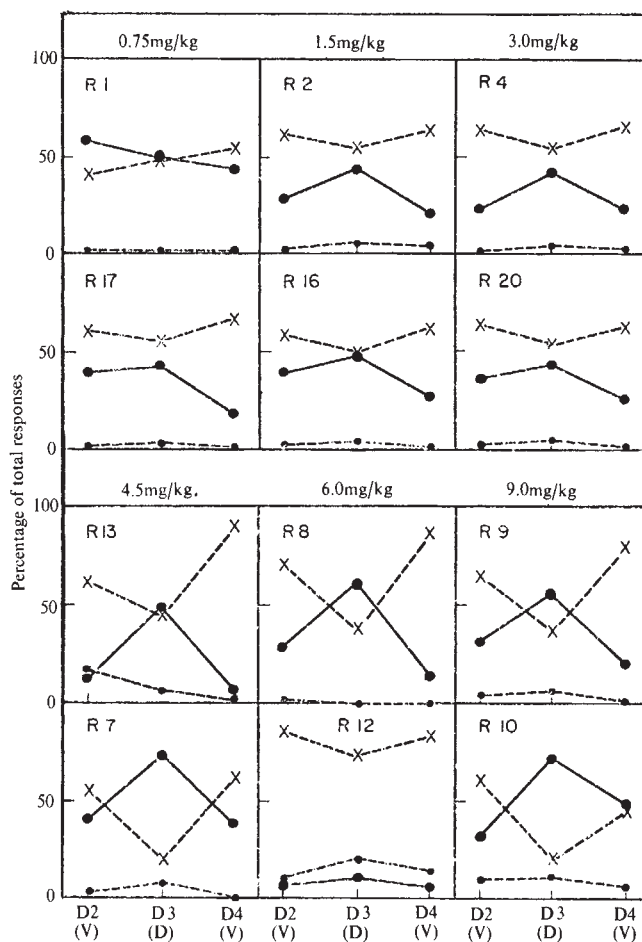


Fig. 3 Modified Bovet-Gatti profiles for twelve rats. Percentage of total responses made in premature interval (●—●), efficient interval (x—x), and late interval (●—●). Vehicle only (V) was injected on pre-drug (D2) and post-drug (D4) days; vehicle plus drug (D) on day 3 (D3).

An experiment of this design cannot be expected to reveal definite dose-response relationships. But preliminary analysis of the data from a more detailed (latin-square) study (described by M. D. W., C. D. W., and B. S. H. at the International Congress of Neuropsychopharmacology, Prague, 1970), although it confirmed the points made here, has failed to reveal any relationship between dose (within a 1.5 to 9.0 mg/kg range), and any of several measures of avoidance performance.

If a drug screening procedure is to be useful in the study of the effects of THC or other hallucinogenic drugs, it must be capable of reflecting subtle changes in behaviour at low dose levels and the particular pattern of change must be reasonably stable from animal to animal and from one drug test to the next. On the basis of the results of the first experiment, it seems that the DRL schedule does not meet either of these requirements when rats are used as subjects. With the discriminated Sidman avoidance schedule used in experiment 2, rats did show definite drug effects at low doses, and the drug

effects were consistent with the main aspects of the Smythies-type avoidance profile for hallucinogens (increased premature and late responding). There was also an overall decrease in response rate only in the DRL situation. This underlines the importance of task variables and, so far, with rats, the discriminated Sidman avoidance baseline has proved to be more sensitive to THC than the DRL effects reported here. In conclusion, our findings run counter to Appel's¹³ statement that positively reinforced behaviour yields more reliable psychomimetic effects at lower doses than does aversively conditioned behaviour.

Parts of this work were supported by research grants to G. C. W. from the National Research Council of Canada and the Ontario Mental Health Foundation. M. D. W. was supported by a Medical Research Council of Canada fellowship. Dr Raphael Mechoulam, School of Pharmacy, Jerusalem, Israel, provided THC. The steroid suspending vehicle was provided by the National Institutes of Health, Bethesda, Maryland. We thank Dr H. K. Kalant for helpful comments, Dr J. A. Carpenter for advice on statistics, and Michael Kocal for technical assistance.

C. D. WEBSTER

Addiction Research Foundation

M. D. WILLINSKY

University of Toronto

BARBARA S. HERRING

Addiction Research Foundation,
344 Bloor Street West,
Toronto 4

G. C. WALTERS

University of Toronto

Received July 28; revised December 14, 1970.

- ¹ Witt, P. N., *Die Wirkung von Substanzen auf den Netzbau der Spinne als Biologischer Test* (Springer, Berlin, 1956).
- ² Abramson, H. A., Gettner, H. H., Hewitt, M. P., and Dean, G., *J. Psychol.*, **52**, 445 (1961).
- ³ Schneider, C. W., and Chenoweth, M. B., *Nature*, **225**, 1262 (1970).
- ⁴ Smythies, J. R., Johnston, V. S., and Bradley, R. J., *Brit. J. Psychiat.*, **115**, 55 (1969).
- ⁵ Mechoulam, R., and Gaoni, Y., *Fortschr. Chem. Organ. Naturstoffe* (edit. by Zeehmeister, L.), **25**, 175 (1967).
- ⁶ Isbell, H., Gorodetzky, C. W., Jasinski, D., Claussen, U., and Korte, F., *Psychopharmacologia*, **11**, 184 (1967).
- ⁷ Hollister, L., Richards, R., and Gillespie, H., *Clin. Pharmacol. Exp. Ther.*, **9**, 6 (1968).
- ⁸ Smythies, J. R., Johnston, V. S., and Bradley, R. J., *Nature*, **216**, 196 (1967).
- ⁹ Zimmerman, J., and Schuster, C. R., *J. Exp. Anal. Behav.*, **5**, 497 (1962).
- ¹⁰ Sidman, M., *J. Comp. Physiol. Psychol.*, **48**, 444 (1955).
- ¹¹ Bovet, D., and Gatti, G. L., in *Pharmacology of Conditioning, Learning and Retention*, 75 (New York, 1965).
- ¹² Smythies, J. R., Johnston, V. S., Bradley, R. J., Bennington, F., Morin, R. D., and Clark, L. C., *Psychopharmacologia*, **10**, 379 (1967).
- ¹³ Appel, J. B., *Psychopharmacology: A Review of Progress 1957-67*, (edit. by Efran, D. H.), 1211 (Public Health Service, 1967).

Mechanism of Internal Stratification of Siliceous Sponge Spicules

BECAUSE sponges constitute an important part of many fossil records, their fine structure should be of interest to palaeontologists. Internal fine structure in spicule fossils would provide a valuable comparison with present day spicules.

Furthermore, changes in the fine structure of spicule fossils may offer clues as to climatological or ecological conditions in that period.

There are two hypotheses to explain the appearance of concentric stratification of siliceous sponge spicules. Bütschli² contends that stratification is due to alternating layers of different refractivity which he surmised is caused by a minute alveolar structure and, on the other hand, Schulze³ maintains that the appearance of stratification represents lamellae of organic matter alternating with siliceous material. The evidence we report supports Bütschli's hypothesis of alternating layers of different refractivity; but this difference seems to be caused not by minute alveoli but by periodically varying amounts of water. Schulze suggested that the concentric stratified structure is probably related to pauses in growth.



Fig. 1 Cross section of a spicule that was heated at 300° for 0.5 h then etched for 30 s in 5% HF. An extensive concentric ring structure is clearly discernible ($\times 8,000$).

We propose that periodic pauses in the growth of a spicule permit the exposed siliceous surface to become highly hydroxylated. When growth resumes the hydroxylated surface becomes incorporated as a stratum of high etch sensitivity and low refractivity giving rise to the concentric stratification revealed by electron and light microscopy¹⁻³. We base this hypothesis on two new observations: first, the etch sensitivity is destroyed by heating above 300° (Fig. 1) but below 600° (Fig. 2); second, water (detected by mass spectrometry) is liberated from spicules during heating in that range (Fig. 3).

Concentric stratification is visible using light optics, but much of the detail is at or beyond the resolution of the light microscope. The following technique was therefore developed to study the fine structure of spicule sections in the electron microscope. Spicules from a siliceous sponge are embedded in epoxy resin. Sections are cut through the sample using a diamond saw so as to expose a maximum number of spicule transverse sections. The sawed surfaces are polished using cerium oxide and cleaned in an ultrasonic cleaner with distilled water. The exposed spicule surfaces are then etched

in an aqueous 5% hydrofluoric acid (HF) solution for 30 s. Cellulose acetate replicating tape is used to prepare negative replicas of the etched surfaces. These are then shadowed at an angle ($\tan^{-1} 0.33$) with platinum and carbon coated in a vacuum evaporator. Plastic is dissolved away with acetone in a vapour condensation washer and the replicas examined in a Siemens Elmiskop I.

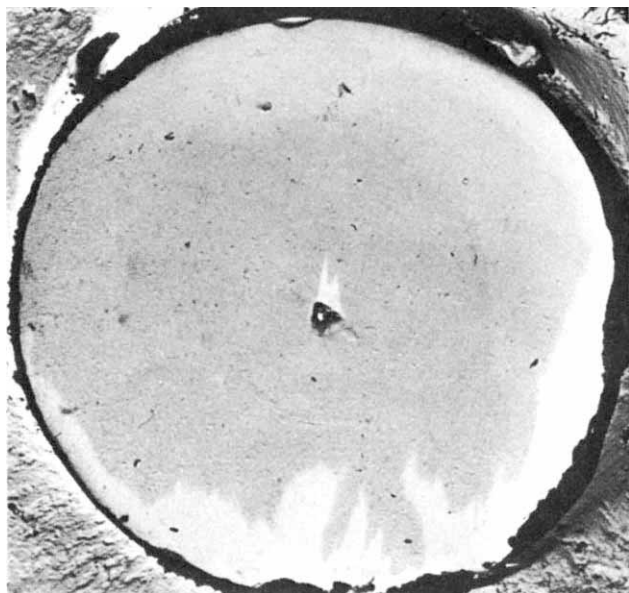


Fig. 2 Cross section of a spicule that was heated at 600° for 0.5 h. The ring structure has been obliterated ($\times 8,000$).

Spicules are formed by specialized scleroblast cells. Growth is believed to be initiated around an organic filament and proceeds by apposition of constituent material^{6,7}. Large siliceous spicules contain an axial filament which has been shown to contain protein⁸. Chemical analyses of *Acarus* spicules indicate that there is enough organic matter present to account for the axial filament¹. The siliceous material immediately surrounding the axial filament is more susceptible to HF attack than the bulk of the spicule. This causes the formation of a conical etch pit which in negative relief appears as a conical spire (Fig. 1). Even though the axial filament is resistant to HF attack, it is not usually preserved using this replica technique.

Fig. 1 shows a transverse section of the major macrosclere (a style $\approx 20 \mu\text{m} \times 340 \mu\text{m}$) from the siliceous sponge *Acarus erithacus*. The replicas are negative impressions of the surface, so that any protrusions or depressions are reversed with respect to the original surface. There are several pronounced rings which probably correspond to those described by earlier investigators using light microscopy of fractured spicules^{2,3}. Between these rings are many finer concentric impressions with spacings as small as 600 Å as measured in high magnification electron micrographs. Unetched spicule sections do not show any ring structure nor is any alveolar structure discernible¹.

Electron micrographs of spicules that are heated for 0.5 h at 300° show that internal structure is not appreciably altered by this treatment. Spicules heated for 0.5 h at 600°, however, no longer have a discernible ring structure (Fig. 2). Thus there seems to be a direct correlation between the loss of water vapour, or more specifically loss of inner constituent hydroxyls, and the obliteration of ring structure within the spicule.

The form of amorphous silica present in sponge spicules is probably that of silica gel⁴. Water content varies from about

6 to 13% corresponding to the formula $(\text{SiO}_2)_{2-5}\text{H}_2\text{O}$. Mass spectrometric analyses show that water vapour is evolved as spicules are heated (Fig. 3). The water peak (mass 18) rapidly rises between 300° and 400° and then drops off between 500° and 600°. Fripiat and Uytterhoeven⁵, from studies involving infrared, thermogravimetric and chemical techniques, were able to distinguish among adsorbed water, surface hydroxyls and inner hydroxyls in commercially prepared silica gel. From these results they hypothesized that inner constituent hydroxyls are evolved at or slightly above 500°, whereas surface adsorbed water hydroxyls are evolved from 180° to 500°. This correlates quite well with our mass spectrometer data since the evolution of water vapour extends within about the same temperature range. Indeed it may even explain what appears to be two separate peaks in the mass spectrometer tracing. The initial peak probably represents surface adsorbed water and hydroxyls while the second peak represents inner hydroxyls.

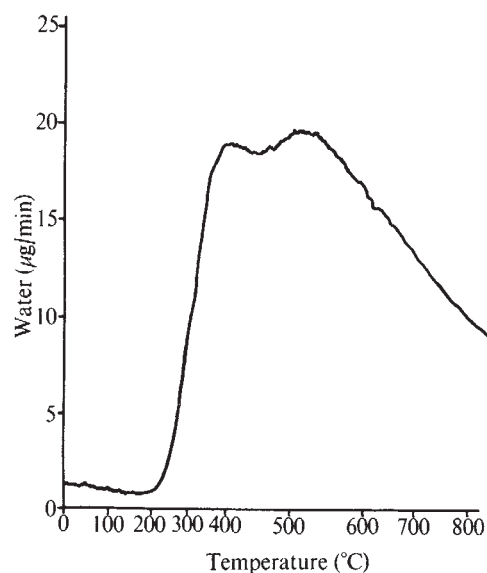


Fig. 3 Mass spectrometric tracing at mass 18 as the spicules are heated to show the evolution of water vapour.

We thank Dr J. Scala and Dr E. J. Hornyak for helpful suggestions and discussion. We also thank Dr R. K. Ware for mass spectrometer analysis.

D. W. SCHWAB

Corporate Research Laboratories,
Owens-Illinois Technical Center,
PO Box 1035,
Toledo, Ohio 43601

R. E. SHORE

Department of Biology,
University of Toledo,
Toledo, Ohio 43606

Received January 7; revised March 22, 1971.

¹ Schwab, D. W., and Shore, R. E., *Biol. Bull.*, **140**, 125 (1971).

² Bütschli, O., *Z. Wiss. Zool.*, **69**, 235 (1901).

³ Schulze, F. E., *Wissenschaftliche Ergebnisse der Deutschen Tiefsee-Expedition auf dem Dampfer "Valdivia" 1898-1899*, **4** (Fischer, Jena, 1904).

⁴ Lewin, J., and Reimann, B. E. F., *Ann. Rev. Plant Physiol.*, **20**, 289 (1969).

⁵ Fripiat, J. J., and Uytterhoeven, J., *J. Phys. Chem.*, **66**, 800 (1962).

⁶ Minchin, E. A., *Proc. Zool. Soc.*, London, **2**, 661 (1908).

⁷ Jørgensen, C. B., *Biol. Medd. Kgl. Dan. Vidensk. Selsk.*, **19**, 1 (1944).

⁸ Garrone, R., *J. Micros.*, **8**, 581 (1969).

BOOK REVIEWS

Biophilosophy

Biophilosophy. By Bernhard Rensch. Translated by C. A. M. Sym. Pp. xi+377. (Columbia University: New York and London, May 1971.) £5.65.

THIS is a valuable book. The author is a distinguished German biologist who has worked in neurology and behaviour studies but is chiefly known as a member of the small international group who made important contributions to the synthetic theory of evolution, his being on *Evolution above the Species Level*, the title of an earlier work available in English (Methuen, London, 1959). People who are interested will find his authoritative, lucid, and up to date discussion of this theory most useful, in particular his "100 rules of infra-specific and trans-specific evolution". This section justifies the volume, which is well translated from the German of 1968.

The greater part of the book presents the author's matured views on more general issues. Science must endeavour to start with absolutely certain facts and these are the mental processes which each of us is aware of within himself, resulting chiefly from perception. It is therefore essential to examine critically the process of cognition by perception, and this leads the author to the problems of mind/matter (he infers a "psycho-physical substratum"), theories and laws, the causal analysis of organisms, and, briefly, free-will, ethics, and religion. Biology, in my view, cannot long avoid coming closer to grips with some of these issues and I expect that many biologists, such as those studying behaviour among others, will find Rensch's analysis helpful, whether or not they go the whole way with him.

Rensch explains that his views are developments of those of Th. Ziehen (1862-1950), and he calls his own attitude "realistic" and "positivist", in special senses which he explains. He infers proto-mental properties from early evolutionary stages onwards, and he assumes not one but many basic laws in physics and biology. As a philosopher Rensch is in some respects original; as an evolutionist he is orthodox and even, for an elsewhere cautious philosopher, a trace dogmatic on points where, clarity being lacking, certainty must be also. He repeatedly asserts the standard view that "random" mutations and the recognized selective processes can together account for the entire

evolutionary process. But he does not, though writing in 1968, explain what "random" means or warn the reader that this central dogma lacks precision until the term has been analysed in the light of the recently acquired knowledge of organic structure, for example in molecular biology.

Adopting the author's own high intellectual standards, one wonders if it is not possible that when morphogenesis—important for evolution theory since selection acts on phenotypes—and the internal coordination and hierarchical structuring of organisms (stressed by him) are better understood, the current formulations of evolution theory may have to be improved to make them more precise and comprehensive. No orthodoxy is aware of all its assumptions, and few remain unchanged when a later generation brings these to light. Great advances often stem from the realization that what has been taken for granted is ambiguous in a new context. Should not a senior biophilosopher bear this in mind for the sake of his young readers to whom this task of clarification may fall?

LANCELOT LAW WHYTE

Memoirs of a Master

Wanderings of a Biochemist. By Fritz Lipmann. Pp. viii+229. (Wiley-Interscience: New York and London, May 1971.) £4.25.

JUST thirty years ago, in the first volume of *Advances in Enzymology*, Fritz Lipmann presented his classic paper on the central roles of energy-rich phosphate compounds and group transfer in biology. How he arrived at these ideas and how they have dominated biochemistry ever since is the central theme of his scientific memoirs in this charming book, his "wanderings".

Lipmann was trained in medicine with a view to going into general practice, but after his final examination he began to question the morality of patients purchasing their health, and doctors selling it. For this and other reasons he drifted away from medicine and returned to his home town of Königsberg in eastern Germany to attend the chemistry courses given in Meerwein's department. From there Lipmann moved to Otto Meyerhof's laboratory in Berlin in 1927.

Two strong personalities dominated

the Kaiser Wilhelm Institute: Otto Meyerhof, a "spiritual presence" who engaged in "unwieldy muscle energetics", and Otto Warburg. The latter, on the top floor of the institute, had a mystery about him, but his "puritanical, pragmatic approach which rejected compromises and speculation filtered through to us from the fourth floor. He became our hero: his stern insistence on letting experiments speak and keeping interpretation to a minimum has dominated our generation". For three years Lipmann dabbled in the biochemistry of phosphorylated intermediates of metabolism, which included some of the hexose phosphates and creatine phosphate, and for this he gained his PhD. Then came a brief collaboration with Lohmann, who at that time had become the master of organic phosphates, classifying them by their very different susceptibilities to acid hydrolysis. Lipmann ended his "biochemical adolescence" with Meyerhof on some important experiments which demonstrated the direct connexion between muscle contraction and the breakdown of creatine phosphate.

The next two years were spent with Albert Fischer in Berlin, and at the Rockefeller University with Levene. In New York he turned his attention to a phospho-protein present in egg yolk and from it isolated serine-phosphate.

In 1932 Lipmann returned to Fischer, now in Copenhagen, as a component of the three big L's of Copenhagen: Linderström-Lang, Lipmann and Lundsgaard. Here he was able to prove that acetyl-phosphate was an intermediate in the oxidative decarboxylation of pyruvic acid and, further, that this phospho-anhydride is used for the enzymatic phosphorylation of adenylic acid. But then the European situation deteriorated and around the middle of 1939 the Lipmanns left Copenhagen for Cornell Medical School, New York. It was here in 1941 that, influenced by the significance of phosphorylation as found by Kalckar, Lundsgaard and others, he developed his ideas on the biosynthetic importance of phosphate derivatives and group transfer.

There are three main points in the review. First, organically-bound phosphates can be divided into two main groups: those with a low energy content and those with a high energy content or "energy-rich". Second, the energy-poor compounds are generally

phosphate esters and arise by transphosphorylation either from an energy-rich or energy-poor phosphate donor. By contrast, energy-rich phosphates are derived by transphosphorylation from an energy-rich donor or by other means, such as oxidative phosphorylation. Third, these phosphorylated compounds, particularly those with high energy bonds, are used for biosynthetic purposes. Lipmann drew a distinction between these two kinds of phosphate bonds by introducing the famous "wriggle" or "squiggle" or $\sim$ P. Among several suggestions, he proposed that perhaps proteins are constructed by polymerization of amino acyl-phosphates: not correct, but not far off either.

The review elicited a very negative response from physical chemists, who regarded the whole concept as dilettantish. Nevertheless, for biochemistry as a whole it was a very major step forward. For the first time a clear distinction had been drawn between the energy requirements of biosynthetic and degradative processes.

Present-day job hunters should take heart: Fritz Lipmann had given a poor talk at an important meeting and, whether or not this was the reason, at this stage of his career he had difficulty in getting a position. Eventually he was accepted in the Department of Surgery at Massachusetts General Hospital, supported by a Ciba fellowship. Fired with high energy phosphate bonds, Lipmann now set out to show that his acetyl-phosphate was the universal acetylating agent. But hard as he tried, acetyl-phosphate did not do the job either in the acetylation of aromatic amines in detoxification, or in the formation of acetylcholine. This led directly to the discovery of a new cofactor, which he called coenzyme A (A for acetylation), in 1947. For this discovery Lipmann later received the Nobel Prize for Medicine.

The general thesis of active phosphates led Lipmann and his colleagues to discover such diverse compounds as carbamyl-phosphate in the synthesis of citrulline and of "active" sulphate, an anhydride of sulphate and adenylic acid (PAPS). Since then they have turned their attention to protein synthesis, being encouraged by their neighbours Hoagland and Zamecnik. Activated amino-acids turned out to be elusive, until Paul Berg found a novel form of active acetate, acetyl-adenylate. Subsequently amino-acyl-adenylates were identified as the true intermediates. During the past several years the Lipmann group, now at the Rockefeller University, has been largely responsible for characterizing the transfer factors needed in bacterial protein synthesis and how GTP is involved in the function of the ribosome.

Lipmann's book is divided into two parts separated by a series of personal photographs. In the first half he describes, often with delectable candour, some of the great scientists who impressed him and how he came to do what he did—a sort of scientific novel which contains a sprinkling of extracts from some of his early papers. The latter part of the book contains several more recent papers, including his Harvey Lecture, delivered in 1948.

Fritz Lipmann's seventieth birthday was celebrated at the 1960 Cold Spring Harbor Symposium on Protein Synthesis. The published volume contains a short appreciation of him which starts "There is no biochemist like Fritz Lipmann. He has always been at the heart of biochemistry". And that story, which should inspire the younger generation, is delightfully told in the *Wanderings of a Biochemist*. MARK S. BRETSCHER

Man Evolves

Man's Natural History. By J. S. Weiner. (The Weidenfeld and Nicolson Natural History.) Pp. xii + 255. (Weidenfeld and Nicolson: London, April 1971.) £3.50.

FOR those who seek a broad view of the biological history of man, and a general understanding of the form and causes of human diversity, there is no better book than this new addition to the Weidenfeld and Nicolson Natural History series. Professor J. S. Weiner has pioneered the modern holistic approach to the study of man; more than anyone else he is responsible for the transformation of physical anthropology from a dry and dusty academic byway, as dead in ideas as the bones with which it was largely concerned, to its present focal position in the human sciences, with relevance to almost every aspect of human existence, and engaged with some of the most exciting scientific problems of today. Weiner's views are simply and well expressed in this book. The approach is an evolutionary one, which is surely the most appropriate for an overall consideration of man's natural history: evolutionary theory provides the integrating framework for human biology as it does for the study of other organisms, and profoundly influences perspectives both in the definition of issues and in subsequent consideration of them.

Weiner, in some detail, first compares man with other higher primates, principally to identify the major trends in hominid evolution, and traces the course of human descent as it is revealed in the fossil record. Here, perforce, attention has to be focused on skeletal material, but this is considered in functional terms, and wherever possible with

reference to what is known or presumed about ecology and behaviour. In recent years, studies of living primates have revealed a vastly greater diversity of form than was previously suspected, and much of this, particularly as it is manifest in locomotor systems, is of focal concern, not only in considering the affinities of man with his closest relatives, but also in attempting to discover the factors for the emergence of the hominids, with their many distinctive features. Concurrent with this increasing interest in form, function and ecology has been a spate of both laboratory and field studies of Primate behaviour. It is still not at all clear how far these studies illuminate our understanding of the origins of human sociality, but few would object to the rather broad but insightful generalizations which Weiner makes.

Following the change from an arboreal to a terrestrial existence, man's ancestors adopted a hunting mode of life. These early terrestrial hominids were confined to tropical regions and probably hunted in the heat of the day, which no doubt explains the remarkable heat tolerance capacity of man. Weiner discusses the nature of this heat tolerance, along with the many other facets of adaptability which are to be found in human physiological systems, but, as here indicated, the viewpoint is ecological. Like other human physiologists he is concerned with the nature of physiological mechanisms, but unlike so many of his colleagues he is also concerned with the effects of physiological systems as they affect and are affected by the daily lives of people.

Weiner, as a physiologist, is also rare in having a deep understanding of genetics, and he discusses at some length in this book the factors which determine the genetic structure of human populations, and which cause geographical diversity in human genetic systems. He also brings together this understanding and his physiological knowledge in interpreting the anthropological history of the various peoples of the world, and never loses sight of the importance of cultural and technological factors, both in considering adaptation to local ecological conditions and in determining the broad course of human history. After all, *Homo sapiens*, in spite of his full range of biological capacity, was still a very rare species until the discovery of technologies which allowed crop cultivation and animal domestication. Today, of course, the problems facing the species are not of rarity, but of overabundance, and in a final chapter called "Towards a World Ecology", Weiner has something to say about this which all who are concerned with the human condition would be advised to read.

G. AINSWORTH HARRISON

Good Development

Developmental Processes in Higher Vertebrates. By R. Bellairs. Pp. xiv + 366. (Logos: London, March 1971.) £6.

IN this book the author provides a modern account of the development of amniotes, that is, of reptiles, birds and mammals or "the higher vertebrates". As far as I know no other similarly specialized treatment is available. For mammals, in particular, there are few general works, because the earlier stages of mammalian development are usually extremely hard to investigate. Most vertebrate developmental biology concerns the Amphibia which are constantly referred to, even in this book.

The first three chapters deal with general concepts; the fourth and fifth with topics special to birds; the sixth with embryonic inductions, mostly in the chick; the seventh and eighth with topics special to the early development of mammals and reptiles respectively; the final four deal with general problems, in particular the mechanisms and control of organ growth, teratology and immunology, and some of the molecular biology of development. I find this organization logical and very satisfactory from the point of view of one trying to understand developmental processes and their control rather than to assimilate experimental minutiae. As there is very little formal structure to the study of development the author is often forced to consider several conflicting explanations of the same process without being able to come to a firm conclusion, that is, she rarely finds it possible to reject an explanation on theoretical grounds. Indeed this reinforces the view that unifying principles such as Wolpert's "positional information" are vital to the development of embryology as a science.

The book contains an extremely useful, factual summary of many aspects of amniote development; it is surprisingly up to date, and it is accurate. The only failing lies in the lack of interpretation of some of the data presented, but I feel that the role of the book is really to stimulate thought and experiment, rather than to supply answers. Thus it should be useful to both theorists and experimentalists and can be recommended to all biologists.

ANTHONY ROBERTSON

Connecting Neurones

Neurons and Interneuronal Connections of the Central Visual System. By E. G. Shkol'nik-Yarros. Translated from the Russian by Basil Haigh. Translation edited by Robert W. Doty. Pp. viii + 295. (Plenum: New York and London, 1971.) \$22.50.

THIS book was originally published in Russian in 1965 and has been revised

and updated by the author for the English edition. Although entitled *Neurons and Interneuronal Connections of the Central Visual System* it is principally concerned with neurones of the visual cortical areas and, to a lesser extent, of the lateral geniculate nucleus. The neurones of these structures are described in considerable detail and several species, ranging from hedgehog to man, are examined. One is fascinated, page after page, to see the drawings of neurones which come in all shapes and sizes, from the well known pyramidal neurones to their less famous brethren, "the parasol" and "semilunar" neurones.

Although the author states somewhat towards the end of the book that "every architectonic characteristic, however trivial, corresponds to a different pattern of interneuronal connections", it is clear from the beginning that he is much impressed by cytoarchitectonic differences, and describes in some detail the different arrangement and types of cells in areas 17, 18 and 19 although it is not clear whose definition of areas 18 and 19, particularly for monkey and man, is used. This limits somewhat the value of the descriptions. It seems a pity that the author should not at least refer to the studies of Lashley and Clark and of von Bonin and Bailey. These authors, to varying degrees, failed to find the cytoarchitectonic differences so confidently described by Brodman (who is mentioned). Having described the cytoarchitectonics and Golgi picture of area 17 and (the undefined) areas 18 and 19, the author gains enough confidence to predict their connexions. For he states that "most association connections originate in areas 18 and 19, which follow from the neuronal structure of these areas... while area 17 is connected principally with subcortical structures and the periphery. This conclusion is also supported by the narrowness of layer III of area 17 in primates". Such a statement may be received with some surprise, for the fact is, of course, that area 17 has abundant association connexions in almost all species described so far.

The most interesting parts of this book are undoubtedly the sections that deal with the structure, shape, dendritic trunks and axonal branchings of the individual cells, but the rigid criteria that we now demand as proof of actual "contact" between cells are, unhappily, missing. The Golgi method, on which the description is largely based, does not and cannot, on its own, allow the identification of interneuronal contacts. The author, for example, believes that axo-axonal contacts exist in the cortex and shows a very unconvincing Golgi photomicrograph to prove his case, although axo-axonal contacts have been extremely difficult to demonstrate in the

cortex by electron microscopy and must be presumed to be very rare, if indeed present at all. Many other types of contacts are described, including connexions between spines and capillaries and axonal swellings and capillaries, almost all based on light microscopy. What was reasonable evidence in Cajal's day is not sufficient evidence now.

The book abounds in speculation, frequently based on scanty anatomical evidence. All the more pity, therefore, that precious little is said of "physiological" cells among which contemporary anatomists feel much more relaxed and at home than among "anatomical" cells such as the "cup-shaped" ones. Nothing is said about "simple" and "complex" cells, for example, although in a final chapter there is much speculation on colour vision as a function of the presence and shapes of specific groups of cells in the visual pathways.

This said, however, the book is bound to have some interest to students of the cortex, if only for the descriptions of the great variety of cells that make up the cortex. In the final analysis, all these different shapes of somata must mean something, just as much as the branching patterns and course of their dendrites and axons do. The book may also help to familiarize scientists in the West with Russian literature on the subject. Much of the material referred to in the book is apparently available in Russian only and therefore presumably unknown to most workers in the West. The highly readable translation will, it is to be hoped, remedy this situation, if only slightly. S. ZEKI

Hydronautics

Hydronautics. Edited by Herman E. Sheets and Victor T. Boatwright, Jr. Pp. xvii + 454. (Academic: New York and London, September 1970.) £10.25.

HYDRONAUTICS is one of those recently-coined words which mean different things to different people. If aeronautics is the art of navigating in the air, then I would have thought that hydronautics should be the art of navigating in (and possibly on) the water: its etymology is certainly this. However, this book (to quote the preface) "treats the major scientific and engineering disciplines related to ocean technology". There are seven chapters each by a different author.

The chapter on ocean resources, by J. H. Clotworthy, is readable, well informed and includes some very sensible comments on potential exploitation. It covers the whole field from petroleum and fish to pollution (a "resource in reverse") and recreation. The only serious fault with this chapter is an almost complete lack of references, which is a pity since he so often succeeds

in arousing one's interest in a topic, but having such a wide field can only deal with it briefly.

In the second chapter F. N. Spiess discusses the oceanic environment as it relates to information gathering and transmission interpreted rather broadly. About two-thirds of the chapter is devoted to acoustics, which is in proportion to its importance, but there are useful sections on electromagnetic systems (including light and infrared), gravitational variations and background radioactivity. This is another well written and informative chapter and it has a good bibliography.

R. L. Wiegel's chapter on ocean dynamics is a great disappointment in that it would be more appropriate to a research review than to a book on marine technology. For example, twenty-five pages are devoted to a scholarly review of the processes of wave generation, but only eighteen lines to the wave climate, which is possibly the most important aspect of ocean dynamics in relation to marine engineering.

The chapter on underwater navigation, by F. A. Andrews, devotes most of its space to acoustic position fixing, but has good descriptions of other navigational aids such as electromagnetic logs, inertia navigation systems and doppler-acoustic navigators.

Dealing with marine vehicles and structures, O. H. Oakley discusses the design of research and survey vessels, floating platforms and submarines. This is a considerable part of the field of naval architecture, and in sixty-four pages means that the treatment is bound to be somewhat superficial. However, it is generally a good introduction to the subject with an adequate bibliography. An important omission is the absence of any discussion of the various modes of failure of pressure hulls.

The subject matter of sea systems by J. P. Craven and P. R. Stang largely duplicates that of other parts of the book, and in particular the previous chapter. One rather feels that "systems" is a popular word at present and that a chapter with this title had to be included even though the editors had no clear idea of what they meant by it. It is written in a pretentious style and adds little to the value of the book.

I am afraid that I have to admit to finding articles on policy generally a bore, particularly when they deal with the principles of planning. It is therefore possibly not H. E. Sheets' fault that I find his chapter on policy planning unreadable.

To sum up, the value of the good chapters in the book is such that they should be read by all students of marine technology, and it is a pity that the high price will stop most individuals from buying it.

M. J. TUCKER

Particulate Systems

The Dynamics of Aerocolloidal Systems. By G. M. Hidy and J. R. Brock. (International Reviews in Aerosol Physics and Chemistry, Vol. 1.) Pp. xv+379. (Pergamon: Oxford and New York, January 1971.) £10; \$27.

THIS book is intended to provide a broad introduction to a new series of reviews in aerosol physics and chemistry, and to be an up to date monograph on the subject of aerosol dynamics. Aerosol scientists who have worked in a field practically devoid of specialist literature until the advent of Fuchs and of Green and Lane (Fuchs, N. A., *Mechanics of Aerosols*; Pergamon, Oxford, 1964; Green, H., and Lane, W., *Particulate Clouds, Dusts and Smokes*; Spon, London, 1964) may find themselves overcome by the amount of literature now appearing, and the prospect of the regular appearance of further books in this series may seem rather daunting.

The chapter titles promise a comprehensive coverage of the subject, but more detailed reading gives the impression that while some topics are dealt with exhaustively, others get only cursory treatment. The scope and limitations of the book are honestly set out in the introduction, where the aim is given "to explore the dynamical behaviour of idealized aerosol particles in the light of modern developments in classical mechanics". Thus there is no reference to the effect of particle shape on aerosol behaviour and no mention of the important recent work of Stöber and others on this subject. This is a pity, for however intellectually satisfying it may be to provide theoretical treatments for the behaviour of spherical particles, they bear little relation to most real life aerosols.

Again, according to the introduction, the effects of electrostatic charging on the particles are taken into account, at least in an elementary fashion. But there is no mention of the charging mechanism or charge distributions or the now classical work of Bricard.

It is inevitable, although perhaps unfair, that this book will be compared with Fuchs and Green and Lane. It adopts a very much more theoretical viewpoint than either of the other two, and although experimental work is very frequently referred to, it is generally quoted quite uncritically and sometimes rather uninformatively.

It will therefore appeal to the theoretician rather than to the experimental physicist. This is perfectly acceptable, and no doubt the series as a whole will give a balanced view of the entire subject.

The errors I found were entirely in the indexing, for example, references to Green, H. and Grad, H. are mixed up. This is unimportant, but there is little

excuse for the misspelling of a particular author's name everywhere it occurs.

W. J. MEGAW

Discrete Astronomy

Relativity and the Question of Discretization. By D. G. B. Edelen and A. G. Wilson. (Springer Tracts in Natural Philosophy, Vol. 20.) Pp. xii+186. (Springer-Verlag: Berlin and New York, 1970.) 38DM; \$10.50.

THE possibility that objects of astronomical interest have a discrete structure has not been seriously considered by many workers in this field, presumably because there is no great body of evidence to support this view. The authors of this book, however—one a mathematician and the other an astronomer—take the minority view and argue for the possibility that the sizes of galaxies form a discrete sequence similar to that found for angular momentum in quantum theory. This they attempt from two different viewpoints, one theoretical and the other observational.

As the title indicates, general relativity provides the framework for the development of the theory in the first section. Consideration is restricted to EO galaxies since a definition of the idea of "size" for these presents fewer problems than for the non-spherical cases, though rather than use the radius to a surface where some physical parameter is specified the authors introduce the concept of a "jump discontinuity". This is physically identified with the surface where galactic space structure gives way to free space. A length scale is derived using this concept, and on the assumption that a parameter appearing in the derivation does not vary from galaxy to galaxy a sequence of possible sizes is obtained. The assumption seems to have no physical basis and to have been made for no reason other than that a discrete set may result, so one is doubtful of the conclusions drawn.

The second part of the book deals with what observational evidence there is to support their view, and starts by examining a sample of thirty-one galaxies for evidence of discretization. It is surprising and disturbing to find that of the two slightly different methods used to obtain linear diameters using redshifts as a distance indicator, one yields significantly discrete diameters and the other does not. Also a surprise is the apparent dependence of the minimum possible diameter on redshift, and an extension of the method indicates discretization of redshifts without being convincing.

The style of writing makes this book difficult to read and tends to obscure rather than clarify the issues. This is not a volume that I feel I should recommend.

R. F. CARSWELL

CORRESPONDENCE

Scientists' Salaries

SIR,—There is already an attitude among administrators that because Fulton is beginning to have an effect professional staff (scientists and the like) can expect their highest rewards by transferring from their basic class to the administrative posts which may become available. (Four of the eight recently appointed Regional Managers in the Ministry of Agriculture were from the professional ranks.) This is surely to be deplored and resisted in that the most valuable scientists and technologists often have more to contribute in their professional work than in any transfer to administrative duties and should expect parity with their administrative colleagues which will now be lost if the present pay award is not altered by arbitration.

Secondly, I must mention a particularly mean action which is being proposed and so far has not been altered by negotiation. It affects a relatively few senior members of the former National Agricultural Advisory Service who transferred from colleges and county councils in 1946 to form the then newly formed service. They were given an undertaking that their retirement age would remain at 65 and this would thus partially compensate them for the loss of pension rights which they suffered in the transfer. (The years of employment prior to 1946 are only counting as half the years in calculating their retirement pensions.)

In the arrangements for the unfortunate reduction in the size of the service, those under 60 are being offered redundancy payments but those over 60 are to retire at once and are thus likely to lose up to five years of salary and 5/80 of their pension payments. The Ministry and, I understand, the Civil Service Department are saying that the undertaking given to these officers when they transferred from their former employment is not legally binding and that they will not therefore provide any redundancy payments for those compelled to retire between the ages of 60 and 65.

(Our correspondent wishes to remain anonymous.)

Baffling Brevity

SIR,—I refer to the conclusion of a letter about mercury pollution¹: "We thank Dr Walter Olszewski, Buffalo General Hospital, for supplying the human brains."

Usually I would fully support your strictures² about superfluous acknowledgments, but here I feel that your readers

must be left baffled by brevity. Are we to believe that Dr Olszewski has made a noble sacrifice to the cause of environmental improvement?—in which case the acknowledgments should surely be bolstered by the George Cross at the very least? Or is it that the authors of the letter are themselves not humans but computers?—a feat of programming for which Dr Olszewski might expect a large award from some electronics firm to supplement the meagre "we thank . . ." from his own creations.

Yours faithfully,

TOM CORREYBACK

3 Church Road,
Potters Bar,
Hertfordshire

¹ Glomski, C. A., Brody, H., and Pillay, S. K. K., *Nature*, **232**, 201 (1971).

² Leading article, *Nature*, **232**, 75 (1971).

Micrometeoroid Muddle

SIR,—I was very pleased to see our work on lunar microcraters and erosion phenomena mentioned (*Nature*, **231**, 492; 1971). Unfortunately, your geomagnetism correspondent fell victim to our unclear terminology. In addition, we were somewhat misquoted.

The terminology in question is the usage of the words "cosmic particles". Unfortunately, this term is in usage by workers in the field of "cosmic dust", "micrometeoroids", etc., as well as by people interested in cosmic and galactic particle tracks. No clear definition exists. In the first case it refers to *solid particles* of minute size. Particles in the 10^{-6} – 10^{-13} g range of extraterrestrial or extralunar origin were described by many workers. In a broader sense the term refers to any solid matter of small grain size in space and therefore the term "cosmic particles" comes into usage. It is synonymous with "cosmic dust", "micrometeoroids", etc.

In the second case the term "cosmic particles" refers to particles on an atomic scale, consisting of high energy radiation of solar or galactic origin, which are more commonly called "cosmic rays".

Over the past 6 months we have become increasingly aware of this problem of terminology and have recently decided to abandon the term "cosmic particles" completely in our work. Instead we use "micrometeoroids" and thus hope to avoid future misunderstandings.

In essence the difference is that of absolute size and/or mass coupled with

vastly different flight velocities. Upon impact on a target, the "micrometeoroids" produce a minute impact crater and the "cosmic rays", due to their increased energy per mass unit, are capable of penetrating solid matter leaving characteristic tracks, *i.e.* lattice defects, etc. Thus both particle types are capable of doing damage to solid matter and are capable of mass removal. Both types of "particle" thus are lunar erosion agents. The quoted paper deals in an indirect way with the effectiveness of the two erosion mechanisms.

Our investigations quoted refer exclusively to phenomena of micrometeoroid impact. We have no data on cosmic rays, nor did we mention their effect on cosmic erosion. At the time of writing (August 1970), no such data were available. The main conclusion at that time was that the prime agent of lunar erosion is the mass removal due to micrometeoroid impact. "Cosmic ray" erosion seemed to be insignificant. Your correspondent misunderstood our reasoning and completely reversed our main conclusion. By now (July 1971), we have a somewhat better feeling for effect of the two erosion agents, and our statements in the *Earth and Planetary Science Letters* paper are substantiated.

Yours faithfully,

FRIEDRICH HORZ

National Aeronautics and
Space Administration,
Manned Spacecraft Center,
Houston,
Texas 77058

Our Geomagnetism Correspondent writes: Notwithstanding Dr Horz's willingness to take much of the responsibility for my misunderstanding, I must apologize to Dr Horz and his colleagues for making the error. My false sense of security was perhaps bolstered by their use of the term *primary* cosmic particles, for "primary" and "secondary" are, of course, adjectives used with specific meaning in cosmic ray studies. On the other hand, it is somewhat of an exaggeration to suggest that I reversed the main conclusion. The same ambiguity in the term "cosmic particles" also led me to suppose (wrongly) that Dr Horz and his colleagues were extending the term "micrometeorites" to cover cosmic rays. Nevertheless, in my interpretation of their conclusion I was careful to distinguish between "cosmic particles" (which I mistakenly called cosmic rays) and secondary ejecta from meteorite impacts—and this was surely the critical distinction, not that between the cosmic rays which were not considered by Dr Horz in the original paper and micrometeorites. Thus I do not think I misunderstood the authors' reasoning, only their terminology. In any event, this correspondence will have been useful if it leads to the avoidance of ambiguity in the future; and I am happy to have the record set straight.

Announcements

University News

James N. Butler, Tyco Laboratories Inc., has been appointed Gordon McKay professor of applied chemistry in the Division of Engineering and Applied Physics at **Harvard University**, and **Philip B. Tomlinson** has been appointed professor of botany.

The title of professor has been conferred on **Dr F. J. Weatherall**, Department of Medicine, **University of Liverpool**.

Dr J. Pitt-Rivers, Ecole Pratique des Hautes Etudes, Paris, has been appointed to the chair of anthropology, London School of Economics, and **Professor J. G. Taylor**, University of Southampton, has been appointed to the chair of mathematics at King's College, London. The following titles have been conferred within the **University of London**: professor of sociology, on **Dr P. S. Cohen**, in respect of his post at the London School of Economics; professor of biochemistry, on **Dr J. B. Pridham**, in respect of his post at Royal Holloway College; professor of chemistry, on **Dr J. H. Ridd**, in respect of his post at University College; professor of mathematics, on **Professor Herman Bondi**, in respect of his post at King's College; professor of bacteriology and immunology, on **Professor D. Gwynne**, in respect of his post at the Lister Institute of Preventive Medicine; professor of chemistry, on **Dr M. L. Tobe**, in respect of his post at University College; professor of nuclear medicine, on **Dr E. S. Williams**, in respect of his post at the Middlesex Hospital Medical School.

Mr V. R. Tindall has been appointed to the chair of obstetrics and gynaecology, **University of Manchester**, in succession to **Professor W. I. C. Morris**.

Dr J. J. Turner, University of Cambridge, has been appointed to the chair of inorganic chemistry at the **University of Newcastle upon Tyne**, and **Dr F. E. Hytten** has been appointed to a personal professorship in human reproductive physiology at that university.

Dr D. L. Gardner has been appointed to the Musgrave chair of pathology and to the directorship of the University Institute of Pathology in the **Queen's University of Belfast**.

Dr Findlay L. Swinton, University of Strathclyde, has been appointed to the second chair in chemistry in the new **University of Ulster**, and **Mr Malcolm Skilbeck**, University of Bristol, has been appointed to the third chair in education.

Appointments

Clayton R. Iverson has been appointed director-general of the **Defence Research Establishment Suffield** at Ralston, Alta., in succession to the late **B. J. Perry**.

Dr N. B. Kreitman has been appointed director of the **MRC Unit for Epidemiological Studies in Psychiatry**, at the Royal Edinburgh Hospital, in succession to **Professor G. M. Carstairs**.

Miscellaneous

Professor George B. Kistiakowsky, Harvard University, has been awarded the Priestley medal of the **American Chemical Society**.

International Meetings

August 26–31, **Stereology**, Berne (Anatomisches Institut, Bülhlstrasse 26, CH-3012, Berne, Switzerland).

September 2–3, **Biochemical Society Meeting**, Brighton (Executive Secretary, The Biochemical Society, 7 Warwick Court, Holborn, London WC1R 5DP).

September 2–4, **Control of Human Ageing**, Rüschlikon-Zürich (John G. Cartwright, Gottlieb Duttweiler Institute for Economic and Social Studies, The Green Meadow Foundation, Rüschlikon-Zürich, Switzerland).

September 13–15, **Surface Chemistry of Oxides**, Uxbridge (The Assistant Secretary, The Faraday Society, 6 Gray's Inn Square, London WC1).

September 15–16, **Plastics in Medicine and Surgery**, Newcastle upon Tyne (A. F. Hall, North Eastern Section Plastics Institute, ICI Agricultural Division, Billingham, Teesside TS23 1LD).

Reports and Publications

not included in the Monthly Books Supplement

Great Britain and Ireland

Experiments in Participation. By George F. Thomason. Pp. 54. (London: Institute of Personnel Management, 1971.) £1. [16]

Proceedings of the Royal Irish Academy. Vol. 71, Section B, No. 7: The Electronic Structures and Stabilities of Hexacarbonylchromium and Nitrogen-pentacarbonylchromium. By William J. Chambera and Noel J. Fitzpatrick. Pp. 97–108. (Dublin: Royal Irish Academy, 1971.) 16p. [16]

BP Statistical Review of the World Oil Industry 1970: Reserves/Production/Consumption/Trade/Refining/Tankers/Energy. Pp. 24. (London: British Petroleum Company, Ltd, 1971.) [26]

Department of Education and Science. Education Survey No. 10: Potential and Progress in a Second Culture—a Survey of the Assessment of Pupils from Overseas. Pp. 38. (London: HMSO, 1971.) 30p net. [26]

The Work of Aslib for the year ended December 1970. Pp. 33. (London: Aslib, 1971.) [26]

Other Countries

Harmonizing Technological Developments and Social Policy in America. (Monograph 11 in a series sponsored by the American Academy of Political and Social Science.) Edited by James C. Charlesworth and Alfred J. Eggers, Jr. Pp. viii + 247. (Philadelphia: American Academy of Political and Social Science, 3937 Chestnut Street, 1970.) \$2. [185]

South Australia. Institute of Medical and Veterinary Science—32nd Annual Report of the Council, July 1969–June 1970. Pp. 62. (Adelaide: Institute of Medical and Veterinary Science, 1971.) [185]

Australia: Commonwealth Scientific and Industrial Research Organization. Report of the Division of Dairy Research for 1970. Pp. 47. (Melbourne: CSIRO, 1971.) [195]

US Department of Agriculture: Agricultural Research Service. General Catalogue of the Homoptera. Index to Genera and Species with Addenda and Corrigenda to Parts 1–17. Fascicle VI: Cicadelloidea. Compiled by Virginia Wade Burnside. Pp. 269. (Washington, DC: Government Printing Office, 1971.) \$1.25. [195]

HOW TO BUY NATURE

Volumes start in January, March, May, July, September and November, but subscriptions may begin at any time.

The direct postal price per subscription is:

12 MONTHS* (52 issues per title)

	Surface Mail UK and worldwide	Airfreight U.S.A.	Canada
Nature (Friday)	£14	\$48	\$52
Nature + Nature Physical Science	£24	\$83	\$90
Nature + Nature New Biology	£24	\$83	\$90
All three editions	£29.50	\$108	\$116
Annual Index	£1	\$3	\$3

* Rates for shorter periods *pro rata* (minimum three months)
(Charge for delivery by air mail on application)

Editorial and Publishing Offices of NATURE

MACMILLAN JOURNALS LIMITED
4 LITTLE ESSEX STREET, LONDON WC2R 3LF
Telephone Number : 01-836 6633. Telegrams : Phusis London WC2R 3LF

711 NATIONAL PRESS BUILDING
WASHINGTON DC 20004
Telephone Number : 202-737 2355

Subscription Department
MACMILLAN JOURNALS LIMITED
BRUNEL ROAD, BASINGSTOKE, HANTS
Telephone Number : Basingstoke 5431

American display advertisements
NATURE SCIENTIFIC PUBLICATIONS INC
711 NATIONAL PRESS BUILDING
WASHINGTON DC 20004

All other advertisements
T. G. SCOTT & SON, LIMITED
1 CLEMENT'S INN, LONDON WC2A 2ED
Telephone : 01-242 6264/01-405 4743
Telegrams : Textualist London WC2A 2ED

Registered as a newspaper at the Post Office

Copyright © Macmillan Journals Limited, August 13 1971